Novel Method and Compounds

This invention relates to a novel method for the treatment and/or prophylaxis of conditions associated with a need for inhibition of glycogen synthase kinase-3 (GSK-3), especially diabetes, including chronic neurodegenerative conditions, including dementias such as Alzheimer's disease, neurotraumatic diseases, such as acute stroke, mood disorders such as schizophrenia and manic depression, and for the treatment and/or prophylaxis of hair loss and cancer, and to certain novel inhibitors of GSK-3 for use in such a method.

GSK-3 is a serine/threonine protein kinase composed of two isoforms (α and β) which are encoded by distinct genes. GSK-3 is one of several protein kinases which phosphorylates glycogen synthase (GS) (Embi *et al* Eur. J. Biochem. **(107)** 519-527 (1980)). The α and β isoforms have a monomeric structure of 49 and 47kD respectively and are both found in mammalian cells. Both isoforms phosphorylate muscle glycogen synthase (Cross *et al* Biochemical Journal **(303)** 21-26 (1994)) and these two isoforms show good homology between species (e.g. human and rabbit GSK-3α are 96% identical).

Type II diabetes (or Non-Insulin Dependent Diabetes Mellitus, NIDDM) is a multifactorial disease. Hyperglycaemia is due to insulin resistance in the liver, muscle and other tissues coupled with inadequate or defective secretion of insulin from pancreatic islets. Skeletal muscle is the major site for insulin-stimulated glucose uptake and in this tissue, glucose removed from the circulation is either metabolised through glycolysis and the TCA cycle, or stored as glycogen. Muscle glycogen deposition plays the more important role in glucose homeostasis and Type II diabetic subjects have defective muscle glycogen storage.

The stimulation of glycogen synthesis by insulin in skeletal muscle results from the dephosphorylation and activation of glycogen synthase (Villar-Palasi C. and Larner J. Biochim. Biophys. Acta **(39)** 171-173 (1960), Parker P J *et al.*, Eur. J. Biochem. **(130)** 227-234 (1983), and Cohen P. Biochem. Soc. Trans. **(21)** 555-567 (1993)). The phosphorylation and dephosphorylation of GS are mediated by specific kinases and phosphatases. GSK-3 is responsible for phosphorylation and deactivation of GS, while glycogen bound protein phosphatase 1 (PP1G) dephosphorylates and activates GS. Insulin both inactivates GSK-3 and activates PP1G (Srivastava A K and Pandey S K Mol. and Cellular Biochem. **(182)** 135-141 (1998)).

Chen *et al.*, Diabetes **(43)** 1234-1241 (1994) found that there was no difference in the mRNA abundance of PP1G between patients with Type II diabetes and control patients, suggesting that an increase in GSK-3 activity might be important in Type II diabetes. It has also recently been demonstrated that GSK-3 is overexpressed in Type II diabetic muscle and that an inverse correlation exists between skeletal muscle GSK-3α activity and insulin action (Nikoulina *et al* Glycogen Synthase Kinase-3 in Human Skeletal Muscle: Relationship To Insulin Resistance in Type II Diabetes. Diabetes **(47(1))** 0028 Page A7 (1998) (Oral presentation)). Overexpression of GSK-3β and constitutively active GSK-3β (S9A, S9E) mutants in HEK-293 cells resulted in

supression of glycogen synthase activity (Eldar-Finkelman *et al.*, PNAS **(93)** 10228-10233 (1996)) and overexpression of GSK-3β in CHO cells, expressing both insulin receptor and insulin receptor substrate 1 (IRS-1), resulted in an impairment of insulin action (Eldar-Finkelman and Krebs PNAS **(94)** 9660-9664 (1997)). Recent evidence for the involvement of elevated GSK-3 activity and the development of insulin resistance and type II diabetes in adipose tissue has emerged from studies undertaken in diabetes and obesity prone C57BL/6J mice (Eldar-Finkelman *et al.*, Diabetes **(48)** 1662-1666 (1999)).

GSK-3 has been shown to phosphorylate other proteins *in vitro* including the eukaryotic initiation factor eIF-2B at $Serine^{540}$ (Welsh *et al.*, FEBS Letts **(421)** 125-130 (1998)). This phosphorylation results in an inhibition of eIF-2B activity and leads to a reduction in this key regulatory step of translation. In disease states, such as diabetes, where there is elevated GSK-3 activity this could result in a reduction of translation and potentially contribute to the pathology of the disease.

Several aspects of GSK-3 functions and regulation in addition to modulation of glycogen synthase activity indicate that inhibitors of this enzyme may be effective in treatment of disorders of the central nervous system. GSK-3 activity is subject to inhibitory phosphorylation by PI 3 kinase-mediated or Wnt-1 class-mediated signals that can be mimicked by treatment with lithium, a low mM inhibitor of GSK-3 (Stambolic V., Ruel L.and Woodgett J.R. Curr. Biol. 1996 6(12): 1664-8).

GSK-3 inhibitors may be of value as neuroprotectants in treatment of acute stroke and other neurotraumatic injuries. Roles for PI 3-kinase signalling through PKB/akt to promote neuronal cell survival are well established, and GSK-3 is one of a number of PKB/akt substrates to be identified that can contribute to the inhibition of apoptosis via this pathway (Pap & Cooper, (1998) J. Biol. Chem. **273:** 19929-19932). Evidence suggests that astrocytic glycogen can provide an alternative energy source to facilitate neuronal survival under conditions of glucose deprivation (for example see Ransom, B.R. and Fern, R. (1997) Glia **21:** 134-141 and references therein). Lithium is known to protect cerebellar granule neurons from death (D'Mello *et al.*, (1994) Exp. Cell Res. **211:** 332-338 and Volonte *et al* (1994) Neurosci. Letts. **172:** 6-10) and chronic lithium treatment has demonstrable efficacy in the middle cerebral artery occlusion model of stroke in rodents (Nonaka and Chuang, (1998) Neuroreport 9(9): 2081-2084). Wnt-induced axonal spreading and branching in neuronal culture models has been shown to correlate with GSK-3 inhibition (Lucas & Salinas, (1997) Dev. Biol. **192:** 31-44) suggesting additional value of GSK-3 inhibitors in promoting neuronal regeneration following neurotraumatic insult.

Tau and β-catenin, two known *in vivo* substrates of GSK-3, are of direct relevance in consideration of further aspects of the value of GSK-3 inhibitors in relation to treatment of chronic neurodegenerative conditions. Tau hyperphosphorylation is an early event in neurodegenerative conditions such as Alzheimer's disease (AD), and is postulated to promote microtubule disassembly. Lithium has been reported to reduce the phosphorylation of tau, enhance the binding of tau to microtubules, and promote microtubule assembly through direct and reversible inhibition of glycogen synthase kinase-3 (Hong M., Chen D.C., Klein P.S. and Lee V.M. J.Biol. Chem. 1997 272(40)

25326-32). β-catenin is phosphorylated by GSK-3 as part of a tripartite complex with axin, resulting in β-catenin being targetted for degradation (Ikeda *et al.*, (1998) EMBO J. **17:** 1371-1384). Inhibition of GSK-3 activity is a key mechanism by which cytosolic levels of catenin are stabilised and hence promote β–catenin-LEF-1/TCF transcriptional activity (Eastman, Grosschedl (1999) Curr. Opin. Cell Biol. **11:** 233). Rapid onset AD mutations in presenilin-1 (PS-1) have been shown to decrease the cytosolic β-catenin pool in transgenic mice. Further evidence suggests that such a reduction in available β-catenin may increase neuronal sensitivity to amyloid mediated death through inhibition of β-catenin-LEF-1/TCF transcriptional regulation of neuroprotective genes (Zhang *et al.*, (1998) Nature **395:** 698-702). A likely mechanism is suggested by the finding that mutant PS-1 protein confers decreased inactivation of GSK-3 compared with normal PS-1 (Weihl, C.C., Ghadge, G.D., Kennedy, S.G., Hay, N., Miller, R.J. and Roos, R.P.(1999) J. Neurosci. **19:** 5360-5369).

WO 97/41854 (University of Pennsylvania) discloses that an effective drug for the treatment of manic depression is lithium, but that there are serious drawbacks associated with this treatment. Whilst the precise mechanism of action of this drug for treatment of manic depression remains to be fully defined, current models suggest that inhibition of GSK-3 is a relevant target that contributes to the modulation of AP-1 DNA binding activity observed with this compound (see Manji *et al.*, (1999) J. Clin. Psychiatry **60** (suppl 2): 27-39 for review).

GSK-3 inhibitors may also be of value in treatment of schizophrenia. Reduced levels of β-catenin have been reported in schizophrenic patients (Cotter D, Kerwin R, al-Sarraji S, Brion JP, Chadwich A, Lovestone S, Anderton B, Everall I. 1998 Neuroreport **9:**1379-1383) and defects in pre-pulse inhibition to startle response have been observed in schizophrenic patients (Swerdlow *et al.*, (1994) Arch. Gen. Psychiat. **51:** 139-154). Mice lacking the adaptor protein dishevelled-1, an essential mediator of Wnt-induced inhibition of GSK-3, exhibit both a behavioural disorder and defects in pre-pulse inhibition to startle response (Lijam N, Paylor R, McDonald MP, Crawley JN, Deng CX, Herrup K, Stevens KE, Maccaferri G, McBain CJ, Sussman DJ, Wynshaw-Boris A. (1997) Cell **90:** 895-905). Together, these findings implicate deregulation of GSK-3 activity as contributing to schizophrenia. Hence, small molecule inhibitors of GSK-3 catalytic activity may be effective in treatment of this mood disorder.

The finding that transient β-catenin stabilisation may play a role in hair development (Gat *et al.*, Cell **(95)** 605-614(1998)) suggests that GSK-3 inhibitors could be used in the treatment of baldness.

Certain substitued 3-amino-4-arylmaleimides are disclosed in Tetrahedron (1998), 54(9), 1745-1752; Liebigs Annalen 1894, 282, 81; BE 659639; J Amer Chem Soc 1958, 80, 1385; J. Prakt. Chem. (1979), 321(5), 787-96; Eur. J. Org. Chem. (1998), (7), 1467-1470; Chem. Heterocycl. Compd. (N. Y.) (1997), 33(1), 69-73; J. Prakt. Chem. (1987), 329(4), 587-91; Collect. Czech. Chem. Commun. (1985), 50(6), 1305-11; Tetrahedron (1984), 40(18), 3499-502; J. Prakt. Chem. (1983), 325(2), 293-300; J Prakt Chem 1983, 325 (2) 293-300; Tetrahedron (1980), 36, 1801-5; which compounds have no disclosed pharmaceutical utility.

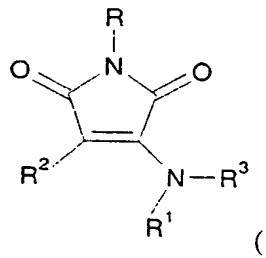
Certain 3-amino-4-arylmaleimides are disclosed in Bioorg. Med. Chem. Lett. (1995), 5(1), 67-72; J. Med. Chem. (1992), 35(1), 177-84; Tetrahedron Lett. (1990), 31(36), 5201-4; EP 328026; Bioorg. Med. Chem. Lett. (1994), 4(24), 2845-50, which compounds are disclosed as being protein kinase C inhibitors or trypanothione reductase inhibitors. Certain 3-amino-4-arylmaleimides are disclosed in DE 4005969 and DE 4005970 as having activity as anti-allergics and immunotherapeutics.

United States Patent Number 3335147 discloses certain 3-amino-4-arylmaleimides as having topical anaesthetic activity. DE 19744257 discloses certain 3-amino-4-arylmaleimides as being tyrosine kinase inhibitors. Chem. Pharm. Bull. (1998), 46(4), 707-710 discloses certain 3-amino-4-arylmaleimides as being trypanothione reductase inhibitors. SA 672268 discloses certain 3-amino-4-arylmaleimides as being antimicrobials.

None of the above mentioned references discloses that the 3-amino-4-arylmaleimides possess GSK-3 inhibitor activity.

We have now discovered that a series of certain 3-amino-4-arylmaleimides are particularly potent and selective inhibitors of GSK-3. These compounds are indicated to be useful for the treatment and/or prophylaxis of conditions associated with a need for inhibition of GSK-3, such as diabetes, chronic neurodegenerative conditions, including dementias such as Alzheimer's disease, manic depression, mood disorders, such as schizophrenia, neurotraumatic diseases, such as acute stroke, hair loss, and cancer. Certain of these compounds are novel and such compounds comprise a further aspect of the invention. In addition, as indicated above it is considered that GSK-3 inhibitors *per se* are potentially useful in the treatment and/or prophylaxis of mood disorders, such as schizophrenia, neurotraumatic diseases, such as acute stroke, and for the treatment and/or prophylaxis of cancer and hair loss .

Accordingly, in a first aspect, the present invention provides a method for the treatment of conditions associated with a need for inhibition of GSK-3, such as diabetes, dementias such as Alzheimer's disease and manic depression which method comprises the administration of a pharmaceutically effective, non-toxic amount of a compound of formula (I):



(I)

or a pharmaceutically acceptable derivative thereof, wherein:

R is hydrogen, alkyl, aryl, or aralkyl;

R^1 is hydrogen, alkyl, aralkyl, hydroxyalkyl or alkoxyalkyl;

R^2 is substituted or unsubstituted aryl or substituted or unsubstituted heterocyclyl;

R^3 is hydrogen, substituted or unsubstituted alkyl, cycloalkyl, alkoxyalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl or aralkyl wherein the aryl moiety is substituted or unsubstituted; or,

R^1 and R^3 together with the nitrogen to which they are attached form a single or fused, optionally substituted, saturated or unsaturated heterocylic ring;

to a human or non-human mammal in need thereof.

Suitably, R is hydrogen, C_{1-6}alkyl, such as methyl or ethyl, or R is phenyl or benzyl.

Preferably, R is hydrogen.

Suitably, R^1 is hydrogen, C_{1-6}alkyl, such as methyl, ethyl, or R^1 is hydroxyethyl or methoxyethyl.

Preferably, R^1 is hydrogen.

When R^2 is substituted or unsubstituted aryl, examples of aryl groups include phenyl and naphthyl.

When R^2 is substituted or unsubstituted heterocyclyl, examples of heterocyclyl groups include indolyl, benzofuranyl, thienyl and benzothienyl.

When R^2 is substituted phenyl, suitable substituents include up to three groups independently selected from halo, C_{1-6}alkoxy, nitro, perfluoroC_{1-6}alkyl, benzoyl, C_{1-6}alkoxycarbonyl, C_{1-6}alkylsulphonyl, hydroxy, $-O(CH_2)_wO-$ where w is 1 to 4, phenoxy, benzyloxy, C_{1-6}alkoxyC_{1-6}alkyl, perfluoroC_{1-6}alkoxy, C_{1-6}alkylS-, perfluoroC_{1-6}alkylS-, (diC_{1-6}alkyl)N-, amino, C_{1-6}alkylcarbonylamino, substituted or unsubstituted ureido, phenylcarbonylamino, benzylcarbonylamino, styrylcarbonylamino, (diC_{1-6}alkoxy)(phenyl)C-, C_{1-6}alkyl, and phenyl.
Suitable substituents for ureido include fluorophenyl, phenylC_{1-6}alkyl-, cyclohexyl, C_{1-6}alkenyl, C_{1-6}alkyl, and C_{1-6}alkoxyphenyl.

When R^2 is substituted indolyl, suitable substituents include C_{1-6}alkyl.

When R^2 is substituted benzothienyl, suitable substituents include C_{1-6}alkyl.

Suitably, R^2 is substituted or unsubstituted phenyl.

Favourably, R^2 is phenyl substituted with:

4-Cl; 3-Cl; 2-Cl; 2,4-di-Cl; 3,4-di-Cl; 3,5-di-Cl; 2,6-di-Cl; 2-F-6-Cl; 2-F; 3-F; 4-F; 2,3-di-F; 2,5-di-F; 2,6-di-F; 3,4-di-F; 3,5-di-F; 2,3,5-tri-F; 3,4,5-tri-F; 2-Br; 3-Br; 4-Br; 2-I; 4-I; 3-Cl-4-OMe; 3-NO_2-4-Cl; 2-OMe-5-Br; 2-NO_2; 3-NO_2; 4-NO_2; 2-CF_3; 3-CF_3; 4-CF_3; 3,5-di-CF_3; 4-PhC(O)-; 4-MeO(O)C-; 4-$MeSO_2$-; 4-OH; 2-OMe; 3-OMe; 4-OMe; 2,4-di-OMe; 2,5-di-OMe; 3,4-di-OMe; 3,4-OCH_2O-; 3,4,5-tri-OMe; 3-NO_2-4-OMe; 4-OnBu; 2-OEt; 2-OPh; 3-OPh; 4-OPh; 2-OCH_2Ph; 4-OCH_2Ph; 4-($MeOCH_2$); 2-OCF_3; 4-OCF_3; 4-SMe; 3-SCF_3; 4-NMe_2; 3-NH_2; 3-(NHC(O)Me); 3-[NHC(O)NH(3-F-Ph)]; 3-[NHC(O)NH$(CH_2)_2$Ph]; 3-[NHC(O)NHCyclohexyl]; 3-[NHC(O)NH$CH_2CH=CH_2$]; 3-[NHC(O)Ph]; 3-[NHC(O)CH_2Ph]; 3-[trans-NHC(O)CH=CHPh]; 3-[NHC(O)nPr]; 3-[NHC(O)NHEt]; 3-[NHC(O)NH(3-OMe-Ph)]; 4-[$C(OMe)_2$Ph]; 2-Me; 3-Me; 4-Me; 4-iPr; 2,5-di-Me; 3,5-di-Me, 4-Ph, 2,3-[(-$CH_2=CH_2$-)], or 3,4-[(-$CH_2=CH_2$-)].

When R^3 is alkyl, examples include methyl and ethyl.

When R^3 is cycloalkyl, examples include cyclohexyl.

When R^3 is alkoxyalkyl, examples include methoxyethyl.

When R^3 is aralkyl, examples include benzyl and phenylethyl.

When R^3 is substituted or unsubstituted aryl, examples include fluorenyl, phenyl, and dibenzofuryl.

When R^3 is substituted or unsubstituted heterocyclyl, examples include thienyl, oxazolyl, benzoxazolyl, pyridyl, and pyrimidinyl.

When R^1 and R^3 together with the nitrogen atom to which they are attached form a fused heterocyclic ring, which ring may be unsubstituted or substituted, examples include indolinyl, indolyl, oxindolyl, benzoxazolinonyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, benzimidazolyl, benzazepinyl, isoindolin-2-yl, and 1,3,3-trimethyl-6-azabicyclo[3.2.1]oct-6-yl.

When R^1 and R^3 together with the nitrogen atom to which they are attached form a single heterocyclic ring, which ring may be unsubstituted or substituted, examples include 1-phenyl-1,3,8-triazaspiro-[4,5]-decan-4-one-8-yl, piperazinyl, pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, and a pyridinium ring.

When R^3 is substituted phenyl, suitable substituents include up to three groups independently selected from substituted or unsubstituted C_{1-6}alkyl, phenyl, benzyl, substituted or unsubstituted C_{1-6}alkylS-, halo, hydroxy, substituted or unsubstituted C_{1-6}alkoxy, substituted or unsubstituted phenoxy, indolyl, naphthyl, carboxy, C_{1-6}alkoxycarbonyl, benzyloxy, pentafluorophenoxy, nitro, N-substituted or unsubstituted carbamoyl, substituted or unsubstituted C_{1-6}alkylcarbonyl, benzoyl, cyano, perfluoroC_{1-6}alkylSO2-, C_{1-6}alkylNHSO$_2$-, oxazolyl, C_{1-6}alkylcarbonylpiperazinyl, substituted or unsubstituted phenylS-, C_{1-6}alkylpiperazinyl-, cyclohexyl, adamantyl, trityl, substituted or unsubstituted C_{1-6}alkenyl, perfluoroC_{1-6}alkyl, perfluoroC_{1-6}alkoxy, perfluoroC_{1-6}alkylS-, aminosulphonyl, alkylaminosulphonyl, dialkylaminosulphonyl, arylaminosulphonyl, morpholino, (diC_{1-6}alkyl)amino, C_{1-6}alkylCONH-, (diC_{1-6}alkoxy)phenyl$(CH_2)_n$NHC(O)CH(phenyl)S- where n is 1 to 6, and C_{1-6}alkylCON(C_{1-6}alkyl)-, thiazolidinedionylC_{1-6}alkyl, phenylCH(OH)-, substituted or unsubstituted piperazinylC_{1-6}alkoxy, substituted or unsubstituted benzoylamino; or –[CH=CH-C(O)O]-, -[(CH=CH)$_2$]-, -[$(CH_2)_x$N(C_{1-6}alkylcarbonyl)]-, -$(CH_2)_x$-, -SCH=N-, -SC(C_{1-6}alkyl)=N-, -OCF$_2$O-, -CH=N-NH-, -CH=CH-NH-, -OC(NHC_{1-6}alkyl)=N-, -OC(O)NH-, -C(O)NC_{1-6}alkylC(O)-, -[CH=CH-CH=N]-, -[CH=C(C_{1-6}alkylcarbonyl)O]-, -C(O)NHC(O)-, -[$(CH_2)_x$C(O)]-, -N=N-NH-, -N=C(C_{1-6}alkyl)O-, -O$(CH_2)_x$O-, -$(CH_2)_x$SO$_2$$(CH_2)_y$-, -N($C_{1-6}$alkylcarbonyl)$(CH_2)_x$- where x and y are independently 1 to 4, pyrimidin-2-yloxy, phenylamino, N-[pyrimidin-2-yl]-N-[C_{1-6}alkyl]amino, C_{1-6}alkylsulphonylamino, and 1,2,3-thiadiazolyl.

Suitable substituents for C_{1-6}alkyl include hydroxy, carboxy, unsubstituted or N-substituted carbamoyl, N-morpholinylcarbonyl, C_{1-6}alkylaminocarbonyl, fluoro, cyano, C_{1-6}alkyl, C_{1-6}alkoxycarbonylamino, amino, C_{1-6}alkylcarbonylamino, benzoylamino, phenylaminocarbonylamino, C_{1-6}alkoxycarbonyl, phosphono.

mono-or bisC_{1-6}alkylphosphonate, C_{1-6}alkylaminosulphonyl, and C_{1-6}alkylcarbonylaminoC_{1-6}alkylaminoCO-.

Suitable substituents for C_{1-6}alkylS- include carboxy, C_{1-6}alkoxycarbonyl, C_{1-6}alkoxyC_{1-6}alkylaminocarbonyl, unsubstituted or N-substituted carbamoyl, and fluoro.

Suitable substituents for C_{1-6}alkoxy include C_{1-6}alkoxy, phenyl, carboxy, C_{1-6}alkoxycarbonyl, unsubstituted or N-substituted carbamoyl, and phenyl.

Suitable substituents for carbamoyl include C_{1-6}alkyl, and C_{1-6}alkoxyC_{1-6}alkyl.

Suitable substituents for C_{1-6}alkylcarbonyl include carboxy, and C_{1-6}alkoxycarbonyl.

Suitable substituents for phenylS- include chloro, nitro, carboxy, C_{1-6}alkylaminocarbonyl, unsubstituted or N-substituted carbamoyl, and C_{1-6}alkoxycarbonyl.

Suitable substituents for C_{1-6}alkenyl include (diC_{1-6}alkyl)aminocarbonyl, carboxy, C_{1-6}alkoxycarbonyl, carbamoyl, and phenyl.

Suitable substituents for piperazinylC_{1-6}alkoxy include methyl.

Suitable substituents for phenoxy include chloro.

Suitable substituents for benzoylamino include hydroxy.

When R^3 is substituted benzofuryl, suitable substituents include C_{1-6}alkylcarbonyl.

When R^3 is substituted thienyl, suitable substituents include C_{1-6}alkylcarbonyl.

When R^3 is substituted oxazolyl, suitable substituents include C_{1-6}alkyl.

When R^3 is substituted benzoxazolyl, suitable substituents include halo.

When R^3 is substituted pyridyl, suitable substituents include up to three substituents independently selected from C_{1-6}alkyl, C_{1-6}alkoxy, and halo.

Suitably, R^3 is substituted or unsubstituted phenyl.

Favourably, R^3 is phenyl substituted with;

2-Me; 2-Et; 2-iPr; 2-CH_2OH; 2-Ph; 2-CH_2Ph; 2-SMe; 2-F; 2-Cl; 2-OH; 2-OMe; 2-OPh; 2-Me-5-F; 2-Me-3-Cl; 2-Me-4-Cl; 2-Me-5-Cl; 2-Me-3-Br; 2,3-di-Me; 2,4-di-Me; 2-Me-4-OH; 2-Me-4-OMe; 2-Me-5-CH_2OH; 2,4,6-tri-Me; 2-(2-Indolyl); (1-Naphthyl); 2-Me-5-COOH; 2-Me-5-COOMe; 2-OH-5-COOH; 2-[$O(CH_2)_2OMe$]-5-[$(CH_2)_2COOH$]; 2-[SCH(Ph)$CONH(CH_2)_2$(3,4-di-OMePh)]; 3-Me; 3-Et; 3-CH_2OH; 3-CH_2OH-6-Me; 3-CH_2OH-4-OMe; 3-(CH_2NMe_2)-4-OMe; 3-[CH_2COOH]; 3-[CH_2COOMe]; 3-[CH_2CONH_2]; 3-[$CH_2CONHMe$]; 3-[CH_2-(thiazolidine-2,4-dion-5-yl)]; 3-SMe; 3-F; 3-Cl; 3-Br; 3-I; 3-CF_3; 3-OH; 3-OMe; 3-OCH_2Ph; 3-OiPr; 3-OPh; 3-O-pentafluorophenyl; 3-(OCH_2CO_2H); 3-(OCH_2CO_2Me); 3-(OCH_2CO_2Et); 3-NO_2; 3-CO_2H; 3-CO_2Me; 3-$CONH_2$; 3-CONHMe; 3-$CONHCH_2CH_2OMe$; 3-COMe; 3-COPh; 3-($COCH_2CH_2CO_2H$); 3-($COCH_2CH_2CO_2Me$); 3-CN; 3-SO_2CF3; 3-SO_2NH-nBu; 3-(5-oxazolyl); 3-[4-methylpiperazin-1-yl]-4-OMe; 3-[O-(pyrimidin-2-yl)]; 3-OH-4-OMe; 3,4-di-OMe; 3,5-di-OMe; 3,4-di-Me; 3,5-di-Me; 3-[trans-CH=CHCONMe$_2$]-4-Cl; 3-F-4-Me; 3-Cl-4-Me; 3-Br-4-Me; 3,5-di-F; 3,4-di-Cl; 3,5-di-Cl; 3,5-di-Br; 3-Cl-4-Br; 3-Cl-4-I; 3-Cl-4-OH; 3-Br-4-OH; 3-F-4-OMe; 3-Cl-4-OMe; 3-Cl-4-SMe; 3-Br-4-Cl; 3-Br-4-OCF_3; 3-Br-5-CF_3; 3,5-di-Cl-4-OH; 3,5-di-Br-4-OH; 3,5-di-Cl-4-Me; 3,5-di-

Br-4-Me; 3-[$CH_2CH(Me)CO_2H$]; 3-CO_2H-4-Cl; 3-CO_2Me-4-Cl; 3-CO_2H-4-OH; 3-$CONH_2$-4-Me; 3-NO_2-4-OH; 3-CO_2H-4-SPh; 3-CO_2H-4-[S-(2-CO_2H-Ph)]; 3-CO_2H-4-[S-(2-CONHMe-Ph)]; 3-CO_2Et-4-[S-(2-CO_2Et-Ph)]; 3-CO_2H-4-[S-(3-CO_2H-Ph)]; 3-CO_2Me-4-[S-(4-Cl-Ph)]; 4-[N(Me)(Pyrimidin-2-yl)]; 4-Me; 4-nBu; 4-tBu; 4-Cyclohexyl; 4-Adamantyl; 4-CPh_3; 4-CH_2CN; 4-CH(OH)Me; 4-CH(OMe)Me; 4-CH_2OH; 4-$CH_2NHC(O)t$-Bu; 4-CH_2NH_2; 4-$CH_2NHCOMe$; 4-$CH_2NHCOPh$; 4-$CH_2NHCONHPh$; 4-CH_2CO_2H; 4-CH_2CO_2Me; 4-[$CH_2P(O)(OH)_2$]; 4-[$CH_2P(O)(OEt)_2$]; 4-[CH_2SO_2NHMe]; 4-$(CH_2)_2OH$; 4-$(CH_2)_2NH_2$; 4-$(CH_2)_2NHCOPh$; 4-$(CH_2)_2NHC(O)Ot$-Bu; 4-[$(CH_2)_2CO_2H$]; 4-[$(CH_2)_2CO_2Me$]; 4-($CH_2CH_2CONH_2$); 4-[$CH_2CH_2CONH(CH_2)_6NHCOMe$]; 4-[$(CH_2)_3CO_2H$]; 4-[$(CH_2)_3CO_2Me$]; 4-[$CH=CH_2$]; 4-($CH=CHCO_2H$); 4-($CH=CHCO_2Et$); 4-($CH=CHCONH_2$); 4-(CH=CHPh); 4-(CH=CH(4-OHPh)); 4-[1,2,3-thiadiazol-4-yl]; 4-[OCH_2-(1-methyl-piperazin-4-yl)]; 4-[4-methylpiperazin-1-yl]; 4-CF_3; 4-SMe; 4-(SCH_2CO_2H); 4-(SCH_2CO_2Me); 4-[$SCH_2CONH(CH_2)_2OMe$]; 4-SCF_3; 4-[S-(4-NO_2-Ph)]; 4-[S-(2-CO_2H-Ph)]; 4-[S-(3-CO_2H-Ph)]; 4-SO_2NH_2; 4-F; 4-Cl; 4-Br; 4-I; 4-OH; 4-OMe; 4-OnBu; 4-OPh; 4-[O-(4-Cl-Ph)]; 4-OCH_2Ph; 4-OCH_2CO_2Me; 4-COPh; 4-COMe; 4-$CONH_2$; 4-CO_2H; 4-CN; 4-NO_2; 4-morpholinyl; 4-[CH_2CO-morpholin-1-yl)]; 4-[$CH_2CONH(CH_2)_2OMe$]; 4-[$(CH_2)_2CONH(CH_2)_6NHC(O)Ot$-Bu]; 4-[$(CH_2)_2CONH(CH_2)_6NH_2$]; 4-[$(CH_2)_2CONH(CH_2)_6NH$-biotinyl]; 4-$NMe_2$; 4-NHCOMe; 4-N(Me)COMe, 2,3-di-F; 4-[NHCO(Ph-2-OH)], 4-(phenylamino); 4-methylsulphonylamino, 2,4-di-F; 2,5-di-F; 2-OMe-3-F; 3-CH_2OMe; 3-CH(OH)Ph; 3,4,-di-F; 3-CO_2H-4-CH_2CO_2H; 3-CO_2H-4-[S-(2-CO_2Et)Ph]; 3-CO_2Et-4-[S-(4-CO_2H)Ph]; 3-CONHMe-4-[S-(2-CONHMe)-Ph]; 3-[4-(dichloroacetyl)piperazin-1-yl]-4-OMe; 4-CH_2CONH_2; 4-SPh; 4-[S-(4-CO_2H-Ph)]; and 4-OCH_2CO_2H.

When R^1 and R^3 together with the nitrogen atom to which they are attached form indolinyl, suitable substituents include C_{1-6}alkyl, perfluoroC_{1-6}alkyl, C_{1-6}alkylSO_2NH-, hydroxyC_{1-6}alkyl, carboxy, C_{1-6}alkoxycarbonyl, C_{1-6}alkoxy, halo, t-butoxycarbonylpiperazin-1-yl, 4-(C_{1-6}alkyl)piperazinyl, piperazinyl, amido, and nitro.

When R^1 and R^3 together with the nitrogen atom to which they are attached form piperazinyl, suitable substituents include alkylcarbonyl, alkyl, or aryl.

When R^1 and R^3 together with the nitrogen atom to which they are attached form tetrahydroquinolinyl, suitable substituents include perfluoroC_{1-6}alkyl.

When R^1 and R^3 together with the nitrogen atom to which they are attached form a pyridinium ring, suitable substituents include amino.

When R^1 and R^3 together with the nitrogen atom to which they are attached form pyrrolidinyl, suitable substituents include hydroxy.

When R^1 and R^3 together with the nitrogen atom to which they are attached form piperidinyl, suitable substituents include benzyl, hydroxyC_{1-6}alkyl, C_{1-6}alkyl, hydroxy, carbamoyl, and C_{1-6}alkoxycarbonyl.

When R^1 and R^3 together with the nitrogen atom to which they are attached form oxindolyl, suitable substituents include C_{1-6}alkyl.

There is a sub-group of compounds, falling wholly within formula (I), and being of formula (IA), wherein R, R^1, R^2 and R^3 are as defined in relation to formula (I), with the proviso that formula (IA) does not include the following compounds, hereinafter referred to as List A:

3-phenyl-4-(4-methylpiperazino)-pyrrole-2,5-dione;
3-[4-(diphenylmethyl)-1-piperazinyl]-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-phenyl-4-(4-phenylpiperazino)-pyrrole-2,5-dione;
1-methyl-3-phenyl-4-(4-phenylpiperazino)-pyrrole-2,5-dione;
1-ethyl-3-phenyl-4-(4-chlorophenylpiperazino)-pyrrole-2,5-dione;
1-allyl-3-phenyl-4-(4-methylpiperazino)-pyrrole-2,5-dione;
3-indol-1-yl-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;
1-(1-methyl-2,5-dioxo-4-phenylamino-2,5-dihydro-1H-pyrrol-3-yl)pyridinium chloride;
1-[1-(4-methyl-pentyl)-2,5-dioxo-4-phenylamino-2,5-dihydro-1H-pyrrol-3-yl]pyridinium chloride;
1-(1-dodecyl-2,5-dioxo-4-phenylamino-2,5-dihydro-1H-pyrrol-3-yl)-pyridinium chloride;
3-[2-benzo[b]thien-2-yl-3-[4-(dimethylamino)-2,5-dihydro-2,5-dioxo-1H-pyrrol-3-yl]-1H-indol-1-yl]-carbamimidothioic acid, propyl ester;
3-(dimethylamino)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-(phenylamino)-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-[[4-(trifluoromethyl)phenyl]amino]-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-(methylamino)-1H-pyrrole-2,5-dione;
3-(1H-imidazo[4,5-b]pyridin-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(6-chloro-9H-purin-9-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(6-amino-9H-purin-9-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-(1H-pyrrolo[2,3-b]pyridin-1-yl)-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-(1-piperidinyl)-1H-pyrrole-2,5-dione;
1-acetyl-3-[2,5-dihydro-1-methyl-2,5-dioxo-4-[[4-(trifluoromethyl)phenyl]amino]-1H-pyrrol-3-yl]-1H-indole;
3-(1H-benzimidazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-benzotriazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-imidazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-indol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-indazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-[3-[(dimethylamino)methyl]-1H-indol-1-yl]-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-benzimidazol-1-yl)-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-(1H-indol-1-yl)-4-(1-methyl-1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-amino-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-amino-4-(5-methoxy-1H-indol-3-yl)-1H-pyrrole-2,5-dione;
1H-Indole-1-carboxylic acid, 3-(4-amino-2,5-dihydro-1-methyl-2,5-dioxo-1H-pyrrol-3-yl)-, 1,1-dimethylethyl ester ;
3-(1H-indol-3-yl)-1-methyl-4-[(phenylmethyl)amino]-1H-pyrrole-2,5-dione;

Glycine, N-[2,5-dihydro-4-(1H-indol-3-yl)-1-methyl-2,5-dioxo-1H-pyrrol-3-yl]-, ethyl ester ;
3-amino-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-[[3-[(3-aminopropyl)amino]propyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
[[3-[4-(3-aminopropyl)-1-piperazinyl]propyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-4-[[3-(4-methyl-1-piperazinyl)propyl]amino]-1H-pyrrole-2,5-dione ;
1-[3-[(3-aminopropyl)amino]propyl]-3-[[3-[(3-aminopropyl)amino]propyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
1-[3-[4-(3-aminopropyl)-1-piperazinyl]propyl]-3-[[3-[4-(3-aminopropyl)-1-piperazinyl]propyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-[3-(4-methyl-1-piperazinyl)propyl]-4-[[3-(4-methyl-1-piperazinyl)propyl]amino]-1H-pyrrole-2,5-dione;
3,3'-[iminobis(3,1-propanediylimino)]bis[4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3,3'-[1,4-piperazinediylbis(3,1-propanediylimino)]bis[4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-[(5-aminopentyl)amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-[[5-[(2-aminoethyl)amino]pentyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-[(2-aminoethyl)amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione ;
3-[(6-aminohexyl)amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione ;
3-[(7-aminoheptyl)amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-[[2-[(2-aminoethyl)amino]ethyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
Benzenepropanamide, .alpha.-amino-N-[5-[[2,5-dihydro-4-(1H-indol-3-yl)-2,5- dioxo-1H-pyrrol-3-yl]amino]pentyl]-, (S)- ;
Pentanoic acid, 4-amino-5-[[5-[[2,5-dihydro-4-(1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]amino]pentyl]amino]-5-oxo-, (S)- ;
Pentanamide, 2-amino-5-[(aminoiminomethyl)amino]-N-[2-[[5-[[2,5-dihydro-4-(1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]amino]pentyl]amino]ethyl]-, (S)-;
Benzenepropanamide, .alpha.-amino-N-[2-[[5-[[2,5-dihydro-4-(1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]amino]pentyl]amino]ethyl]-, (S)- ;
Butanamide, 4-[(aminoiminomethyl)amino]-N-[5-[[2,5-dihydro-4-(1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]amino]pentyl]-, (S)- ;
3-phenyl-4-(diethylamino)-pyrrole-2,5-dione;
3-phenyl-4-(benzylamino)-pyrrole-2,5-dione;
1-methyl-3-phenyl-4-(2-diethylaminoethylamino)-pyrrole-2,5-dione;
1-allyl-3-phenyl-4-(2-dimethylaminoethylamino)-pyrrole-2,5-dione; and;
1,3-diphenyl-4-piperidino-pyrrole-2,5-dione.

There is a further sub-group of compounds, falling wholly within formula (I), and being of formula (IB), wherein R, R^1, R^2 and R^3 are as defined in relation to formula (I), with the proviso that formula (IB) does not include the following compounds, hereinafter referred to as List B:
3-(4-methylpiperazin-l-yl)-4-phenyl-pyrrole-2,5-dione;
3-(4-ethylpiperazin-l-yl)-4-phenyl-pyrrole-2,5-dione;

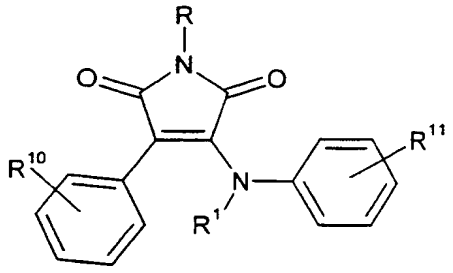
3-(4-chlorophenyl)-4-(4-methyl-piperazin-l-yl)-pyrrole-2,5-dione;
3-[4-(diphenylmethyl)-1-piperazinyl]-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-phenyl-4-(4-methylpiperazino)-pyrrole-2,5-dione;
3-phenyl-4-(4-phenylpiperazino)-pyrrole-2,5-dione;
1-methyl-3-phenyl-4-(4-phenylpiperazino)-pyrrole-2,5-dione;
1-ethyl-3-phenyl-4-(4-chlorophenylpiperazino)-pyrrole-2,5-dione;
1-allyl-3-phenyl-4-(4-methylpiperazino)-pyrrole-2,5-dione;
3-phenylamino-4-phenyl-1H-pyrrole-2,5-dione;
3-phenyl-4-piperidin-1-yl-pyrrole-2,5-dione;
3-(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)-4-morpholin-4-yl-pyrrole-2,5-dione;
3-indol-1-yl-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;
1-(1-methyl-2,5-dioxo-4-phenylamino-2,5-dihydro-1H-pyrrol-3-yl)-pyridinium chloride;
1-1-(4-methyl-pentyl)-2,5-dioxo-4-phenylamino-2,5-dihydro-1H-pyrrol-3-yl)-pyridinium chloride;
1-(1-dodecyl-2,5-dioxo-4-phenylamino-2,5-dihydro-1H-pyrrol-3-yl)-pyridinium chloride;
3-[2,5-dihydro-4-(1H-imidazol-1-yl)-1-methyl-2,5-dioxo-1H-pyrrol-3-yl]-1H-indole-1-carboxylic acid, 1,1-dimethylethyl ester;
3-[2-benzo[b]thien-2-yl-3-[4-(dimethylamino)-2,5-dihydro-2,5-dioxo-1H-pyrrol-3-yl]-1H-indol-1-yl]-carbamimidothioic acid, propyl ester;
3-(dimethylamino)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-(phenylamino)-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-[[4-(trifluoromethyl)phenyl]amino]-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-(methylamino)-1H-pyrrole-2,5-dione;
3-(1H-imidazo[4,5-b]pyridin-l-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(6-chloro-9H-purin-9-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(6-amino-9H-purin-9-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-(1H-pyrrolo[2,3-b]pyridin-1-yl)-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-(1-piperidinyl)-1H-pyrrole-2,5-dione;
1-acetyl-3-[2,5-dihydro-1-methyl-2,5-dioxo-4-[[4-(trifluoromethyl)phenyl]amino]-1H-pyrrol-3-yl]-1H-indole;
3-(1H-benzimidazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-benzotriazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-imidazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-indol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-indazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-[3-[(dimethylamino)methyl]-1H-indol-1-yl]-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-benzimidazol-1-yl)-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-(1H-indol-1-yl)-4-(1-methyl-1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)-4-(4-morpholinyl)-1H-pyrrole-2,5-dione;
3-amino-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-amino-4-(5-methoxy-1H-indol-3-yl)-1H-pyrrole-2,5-dione;

1H-Indole-1-carboxylic acid, 3-(4-amino-2,5-dihydro-1-methyl-2,5-dioxo-1H-pyrrol-3-yl)-, 1,1-dimethylethyl ester ;
3-(1H-indol-3-yl)-1-methyl-4-[(phenylmethyl)amino]-1H-pyrrole-2,5-dione;
Glycine, N-[2,5-dihydro-4-(1H-indol-3-yl)-1-methyl-2,5-dioxo-1H-pyrrol-3-yl]-, ethyl ester ;
3-amino-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
1-(4-methylphenyl)-3-[(4-methylphenyl)amino]-4-phenyl-1H-pyrrole-2,5-dione ;
3-[[3-[(3-aminopropyl)amino]propyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione ;
3-[[3-[4-(3-aminopropyl)-1-piperazinyl]propyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-4-[[3-(4-methyl-1-piperazinyl)propyl]amino]-1H-pyrrole-2,5-dione ;
1-[3-[(3-aminopropyl)amino]propyl]-3-[[3-[(3-aminopropyl)amino]propyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
1-[3-[4-(3-aminopropyl)-1-piperazinyl]propyl]-3-[[3-[4-(3-aminopropyl)-1-piperazinyl]propyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-[3-(4-methyl-1-piperazinyl)propyl]-4-[[3-(4-methyl-1-piperazinyl)propyl]amino]- 1H-pyrrole-2,5-dione;
3,3'-[iminobis(3,1-propanediylimino)]bis[4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3,3'-[1,4-piperazinediylbis(3,1-propanediylimino)]bis[4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-amino-4-(3,4-dimethoxyphenyl)-1H-pyrrole-2,5-dione ;
3-[(5-aminopentyl)amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-[[5-[(2-aminoethyl)amino]pentyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-[(2-aminoethyl)amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-[(6-aminohexyl)amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione ;
3-[(7-aminoheptyl)amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-[[2-[(2-aminoethyl)amino]ethyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
Benzenepropanamide, .alpha.-amino-N-[5-[[2,5-dihydro-4-(1H-indol-3-yl)-2,5- dioxo-1H-pyrrol-3-yl]amino]pentyl]-, (S)- ;
Pentanoic acid, 4-amino-5-[[5-[[2,5-dihydro-4-(1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]amino]pentyl]amino]-5-oxo-, (S)- ;
Pentanamide, 2-amino-5-[(aminoiminomethyl)amino]-N-[2-[[5-[[2,5-dihydro-4-(1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]amino]pentyl]amino]ethyl]-, (S)-;
Benzenepropanamide, .alpha.-amino-N-[2-[[5-[[2,5-dihydro-4-(1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]amino]pentyl]amino]ethyl]-, (S)- ;
Butanamide, 4-[(aminoiminomethyl)amino]-N-[5-[[2,5-dihydro-4-(1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]amino]pentyl]-, (S)- ;
3-(4-methylphenyl)-1-phenyl-4-(phenylamino)-1H-pyrrole-2,5-dione;
1,3-bis(4-methylphenyl)-4-[(4-methylphenyl)amino]-1H-pyrrole-2,5-dione;p
3-amino-1,4-diphenyl-1H-pyrrole-2,5-dione;
3-(4-methylphenyl)-4-(4-morpholinyl)-1-phenyl-1H-pyrrole-2,5-dione ;
3-(4-methylphenyl)-1-phenyl-4-[(phenylmethyl)amino]-1H-pyrrole-2,5-dione;
3-amino-4-(4-methylphenyl)-1-phenyl-1H-pyrrole-2,5-dione ;

3-(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)-4-(4-morpholinyl)-1H-pyrrole-2,5-dione;
3-(4-nitrophenyl)-1-phenyl-4-phenylamino-1H-pyrrole-2,5-dione ;
3-amino-1-methyl-4-p-tolyl-1H-pyrrole-2,5-dione;
3-(2-diethylamino-ethylamino)-4-phenyl-pyrrole-2,5-dione;
3-[butyl-(2-diethylamino-ethyl)-amino]-4-phenyl-pyrrole-2,5-dione;
3-[benzyl-(2-dimethylamino-ethyl)-amino]-4-phenyl-pyrrole-2,5-dione;
3-[benzyl-(2-dimethylamino-ethyl)-amino]-1-methyl-4-phenyl-pyrrole-2,5-dione;
3-[benzyl-(2-dimethylamino-ethyl)-amino]-4-(4-chloro-phenyl)-pyrrole-2,5-dione;
3-[benzyl-(2-diethylamino-ethyl)-amino]-4-phenyl-pyrrole-2,5-dione;
3-[benzyl-(2-dimethylamino-ethyl)-amino]-4-(3-methoxy-phenyl)-pyrrole-2,5-dione;
3-(4-chloro-phenyl)-4-[2-(4-methyl-piperazin-1-yl)-ethylamino]-pyrrole-2,5-dione;
3-[2-(4-methyl-piperazin-1-yl)-ethylamino]-4-phenyl-pyrrole-2,5-dione;
3-phenyl-4-(diethylamino)-pyrrole-2,5-dione;
3-phenyl-4-(benzylamino)-pyrrole-2,5-dione;
1-methyl-3-phenyl-4-(2-diethylaminoethylamino)-pyrrole-2,5-dione;
1-allyl-3-phenyl-4-(2-dimethylaminoethylamino)-pyrrole-2,5-dione; and;
1,3-diphenyl-4-piperidino-pyrrole-2,5-dione.

It is considered that the compounds of formula (IB) are novel. Accordingly , the present invention also provides a compound of the above defined formula (IB) or a derivative thereof.

There is a subgroup of compounds falling wholly within formula (I) of formula (IC):



(IC)

wherein;

R and R^1 are as defined in relation to formula (I);

R^{10} represents hydrogen or one or more substituents, suitably up to three, selected from the list consisting of: alkoxycarbonyl, alkoxyalkyl, perfluoroalkyl, perfluoroalkylS-, perfluoroalkylO-, phenyl(di-C_{1-6}alkoxy)C-, benzoyl, C_{1-6}alkylSO_2-, -[(CH=CH)$_2$]-, phenyl, nitro, -OCH_2O-, benzyloxy, phenoxy, halo, hydroxy, alkyl, alkoxy, amino, mono- or di-alkyl amino or thioalkyl;

R^{11} represents hydrogen or one or more substituents, suitably up to three, selected from the list consisting of: substituted or unsubstituted C_{1-6}alkyl, phenyl, benzyl, substituted or unsubstituted C_{1-6}alkylS-, halo, hydroxy, substituted or unsubstituted C_{1-6}alkoxy, substituted or unsubstituted phenoxy, indolyl, naphthyl, carboxy, C_{1-}

$_6$alkoxycarbonyl, benzyloxy, phenoxy, pentafluorophenoxy, nitro, substituted or unsubstituted carbamoyl, substituted or unsubstituted C_{1-6}alkylcarbonyl, benzoyl, cyano, perfluoroC_{1-6}alkylSO_2-, C_{1-6}alkylNHSO_2-, oxazolyl, substituted or unsubstituted phenylS-, C_{1-6}alkylpiperazinyl-, C_{1-6}alkylcarbonylpiperazinyl-, 1,2,3-thiadiazolyl, pyrimidin-2-yloxy, N-[pyrimidin-2-yl]-N-methylamino, phenylamino, C_{1-6}alkylsulphonylamino, N-morpholinylcarbonyl, cyclohexyl, adamantyl, trityl, substituted or unsubstituted C_{1-6}alkenyl, perfluoroC_{1-6}alkyl, perfluoroC_{1-6}alkoxy, perfluoroC_{1-6}alkylS-, aminosulphonyl, morpholino, (diC_{1-6}alkyl)amino, C_{1-6}alkylCONH-, (diC_{1-6}alkoxy)phenyl$(CH_2)_n$NHC(O)CH(phenyl)S- where n is 1 to 6, and C_{1-6}alkylCON(C_{1-6}alkyl)-, thiazolidinedionylC_{1-6}alkyl, phenylCH(OH)-, substituted or unsubstituted piperazinylC_{1-6}alkoxy, substituted or unsubstituted benzoylamino;
or $-(CH_2)_x-$, -SCH=N-, -SC(C_{1-6}alkyl)=N-, $-OCF_2O-$, -[CH=CHC(O)O]-, -[N=CH-CH=CH]-, -CH=N-NH-, -CH=CH-NH-, -OC(NHC_{1-6}alkyl)=N-, -OC(O)NH-, -C(O)NMeC(O)-, -C(O)NHC(O)-, $-(CH_2)_xC(O)-$, -N=N-NH-, -N=C(C_{1-6}alkyl)O-, $-O(CH_2)_xO-$, $-(CH_2)_xSO_2(CH_2)_y-$,
and -N(C_{1-6}alkylcarbonyl)$(CH_2)_x-$, where x and y are independently 1 to 4.

There is a subgroup of compounds within formula (IC) of formula (IC') wherein R, R^1, R^{10} and R^{11} are as defined in relation to formula (IC) with the proviso that formula (IC') does not include:
3-phenylamino-4-phenyl-1H-pyrrole-2,5-dione;
1-(4-methylphenyl)-3-[(4-methylphenyl)amino]-4-phenyl-1H-pyrrole-2,5-dione;
3-(4-methylphenyl)-1-phenyl-4-(phenylamino)-1H-pyrrole-2,5-dione;
1,3-bis(4-methylphenyl)-4-[(4-methylphenyl)amino]-1H-yrrole-2,5-dione, or;
3-(4-nitrophenyl)-1-phenyl-4-phenylamino-1H-pyrrole-2,5-dione.

Suitably, R is hydrogen.

Suitably, R^1 is hydrogen.

Suitably, R^{10} represents hydrogen or one or more substituents selected from the list consisting of: halo, hydroxy, alkyl, alkylthio, alkoxy, amino or methylenedioxy, especially one or more halo and alkyl groups.

Favourably, R^{10} represents hydrogen or the substituents selected from the list consisting of: 2-Br, 2-Cl, 2-F, 2-OMe, 3-Cl, 3-F, 3-Me, 3-NH_2, 3-OMe, 4-Br, 4-Cl, 4-I, 4-Me, 4-OH, 4-OMe, 4-SMe, 2,3-di-F, 2,5-di-F, 2,6-di-F, 3,4-di-F, 3,5-di-F, 2,3,5-tri-F, 2,4-di-Cl, 2,4-di-OMe, 3,4-(OCH_2O) and 3,5-di-Me.

More favourably, R^{10} represents the substituents selected from the list consisting of: 2-Br, 2-Cl, 2-F, 2-OMe, 3-Cl, 3-F, 3-Me, 4-Br, 4-Cl, 4-I, 2,3-di-F, 2,5-di-F, 2,6-di-F, 3,4-di-F, 3,5-di-F, 2,3,5-tri-F, 2,4-di-Cl and 3,5-di-Me.

Preferably, R^{10} represents the substituents selected from the list consisting of: 2-F, 2-OMe, 3-F, 4-Cl and 2,3-di-F.

Suitably, R^{11} represents hydrogen or one or more substituents selected from the list consisting of: 2-F, 2-Me, 3-Br, 3-Cl , 3-F, 3-I, 3-OH, 3-OMe, 3-OPh, 3-SMe, 3-

CO_2H, 3-CH_2CO_2H, 3-CH_2CO_2Me, 3-CH_2CONH_2, 3-$CH_2CONHMe$, 3-CH_2OH, 4-Cl, 4-F, 4-Me, 4-NHCOMe, 4-NHPh, 4-$NHSO_2Me$, 4-NMe_2, 4-OMe, 4-COPh, 4-SMe, 4-CH_2CN, 4-SO_2NH_2, 4-$(CH_2)_2OH$, 4-CH(OH)Ph, 4-CH_2SO_2NHMe, 4-CH_2CO_2H, 4-$(CH_2)_2CO_2H$, 4-$(CH_2)_2CO_2Me$, 4-$(CH_2)_2CONH_2$, 4-$(CH_2)_3CO_2H$, 4-$(CH_2)_3CONH_2$, 4-CH=CHCO$_2$H, 4-CH=CHCONH$_2$, 4-OCH_2CO_2H, 4-SCH_2CO_2H, 4-S-[2-CO_2H-Ph], 4-S-[3-CO_2H-Ph], 4-CH_2(1,3-thiazolidin-2,4-dion-5-yl), 2,3-di-F, 2,4-di-F, 3,4-di-F, 3,5-di-F, 3-Cl-4-Br, 3-Cl-4-Me, 3-Br-4-Me, 3-Cl-4-OH, 3-Cl-4-OMe, 3,5-di-Me, 3,5-di-OMe, 3,4-OC(O)NH-, 3,4-OCF_2O-, 3,5-di-Br-4-OH, 3,5-di-Cl-4-Me, 3,5-di-Cl-4-OH, 3-CO_2H-4-[S-(2-CO_2H)-Ph], 3-CO_2H-4-[S-(2-CONHMe)-Ph], 3-CO_2H-4-Cl, 3-F-4-Me, 3-F-4-OMe, -3,4-[(CH=N-NH)]-, -3,4-[(N=N-NH)]-, -3,4-[(NH-N=CH)]-, -3,4-[$(CH_2)_3$]-, -3,4-[$(O(CH_2)_3O)$]-, -3,4-[O-C(NHMe)=N]-, -3,4-[OCH_2O]-, -3,4-[S-C(NHMe)=N]- and -3,4-[S-CH=N]-.

Favourably, R^{11} represents hydrogen or the substituents selected from the list consisting of: 2-F, 2-Me, 3-Cl , 3-F, 3-I, 3-OMe, 3-OPh, 3-SMe, 3-CH_2CO_2H, 3-CH_2CO_2Me, 3-CH_2CONH_2, 3-$CH_2CONHMe$, 3-CH_2OH, 4-Cl, 4-F, 4-Me, 4-NHCOMe, 4-NHPh, 4-$NHSO_2Me$, 4-NMe_2, 4-OMe, 4-COPh, 4-SMe, 4-CH_2CN, 4-SO_2NH_2, 4-$(CH_2)_2OH$, 4-CH(OH)Ph, 4- CH_2SO_2NHMe, 4-CH_2CO_2H, 4-$(CH_2)_2CO_2H$, 4-$(CH_2)_2CO_2Me$, 4-$(CH_2)_2CONH_2$, 4-$(CH_2)_3CO_2H$, 4-$(CH_2)_3CONH_2$, 4-CH=CHCONH$_2$, 4-OCH_2CO_2H, 4-SCH_2CO_2H, 4-S-[2-CO_2H-Ph], 4-S-[3-CO_2H-Ph], 4-CH_2 (1,3-thiazolidin-2,4-dion-5-yl), 2,3-di-F, 2,4-di-F, 3,4-di-F, 3,5-di-F, 3-Cl-4-Br, 3-Cl-4-Me, 3-Br-4-Me, 3-Cl-4-OH, 3-Cl-4-OMe, 3,5-di-Me, 3,5-di-OMe, 3,4-[OC(O)NH], 3,4-[OCF_2O] 3,5-di-Cl-4-Me, 3-CO_2H-4-[S-(2-CONHMe)-Ph], 3-F-4-Me, 3-F-4-OMe, 3,4-[(CH=N-NH)], 3,4-[(N=N-NH)], 3,4-[(NH-N=CH)], 3,4-[$(CH_2)_3$], 3,4-[$O(CH_2)_3O$], 3,4-[O-C(NHMe)=N], 3,4-[OCH_2O], 3,4-[S-C(NHMe)=N] and 3,4-[S-CH=N].

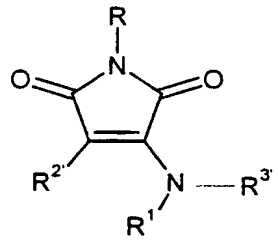
More favourably, R^{11} represents the substituents selected from the list consisting of: 3-Cl , 3-Br, 4-OMe, 3,5-di-F, 4-CH_2SO_2NHMe, 4-$(CH_2)_3CO_2H$ and 4-S-[3-CO_2H-Ph].

A particular compound of formula (IC) is that wherein R and R^1 each represent hydrogen and R^{10} and R^{11} each have the following respective values:

R^{10}	R11
4-Cl	3-Cl
4-Cl	3-Br
2-OMe	4-OMe
4-Cl	4-CH_2SO_2NHMe
2-OMe	3,5-di-F
2-F	3,5-di-F
3-F	4-$(CH_2)_3CO_2H$
2,3-di-F-Ph	3,5-di-F.

It is considered that the compounds of formula (IC') are novel. Accordingly , the present invention also provides a compound of the above defined formula (IC') or a derivative thereof.

There is a subgroup of compounds falling wholly within formula (I) being of formula (ID):



(ID)

wherein R and R^1 are as defined in relation to formula (I);

$R^{2'}$ is phenyl, substituted phenyl or indolyl;

$R^{3'}$ is hydrogen, alkyl, cycloalkyl, phenyl, substituted phenyl, C_{1-6} alkylphenyl wherein the phenyl group is optionally substituted, alkoxyalkyl, substituted or unsubstituted heterocyclyl.

In one aspect, there is provided a compound of formula (I) as hereinbefore defined which excludes compounds of formula (ID).

There is a subgroup of compounds within formula (ID) of formula (ID') wherein R, R^1, $R^{2'}$ and $R^{3'}$ are as defined in relation to formula (ID) with the proviso that formula (ID') does not include the following compounds, hereinafter referred to as List D':

3-[2-benzo[b]thien-2-yl-3-[4-(dimethylamino)-2,5-dihydro-2,5-dioxo-1H-pyrrol-3-yl]-1H-indol-1-yl]-carbamimidothioic acid,propyl ester;

3-(dimethylamino)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;

3-(1H-indol-3-yl)-1-methyl-4-(phenylamino)-1H-pyrrole-2,5-dione;

3-(1H-indol-3-yl)-1-methyl-4-[[4-(trifluoromethyl)phenyl]amino]-1H-pyrrole-2,5-dione;

3-(1H-indol-3-yl)-1-methyl-4-(methylamino)-1H-pyrrole-2,5-dione;

3-(6-chloro-9H-purin-9-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;

3-(6-amino-9H-purin-9-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;

1-acetyl-3-[2,5-dihydro-1-methyl-2,5-dioxo-4-[[4-(trifluoromethyl)phenyl]amino]-1H-pyrrol-3-yl]-1H-indole;

3-amino-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;

3-amino-4-(5-methoxy-1H-indol-3-yl)- 1H-pyrrole-2,5-dione;

1H-Indole-1-carboxylic acid, 3-(4-amino-2,5-dihydro-1-methyl-2,5-dioxo-1H-pyrrol-3-yl)-, 1,1-dimethylethyl ester;

3-(1H-indol-3-yl)-1-methyl-4-[(phenylmethyl)amino]-1H-pyrrole-2,5-dione;

Glycine, N-[2,5-dihydro-4-(1H-indol-3-yl)-1-methyl-2,5-dioxo-1H-pyrrol-3-yl]-, ethyl ester;

3-amino-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;

3-[[3-[(3-aminopropyl)amino]propyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;

3-[[3-[4-(3-aminopropyl)-1-piperazinyl]propyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-4-[[3-(4-methyl-1-piperazinyl)propyl]amino]-1H-pyrrole-2,5-dione;
1-[3-[(3-aminopropyl)amino]propyl]-3-[[3-[(3-aminopropyl)amino]propyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
1-[3-[4-(3-aminopropyl)-1-piperazinyl]propyl]-3-[[3-[4-(3-aminopropyl)-1-piperazinyl]propyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-[3-(4-methyl-1-piperazinyl)propyl]-4-[[3-(4-methyl-1-piperazinyl)propyl]amino]-1H-pyrrole-2,5-dione;
3,3'-[iminobis(3,1-propanediylimino)]bis[4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3,3'-[1,4-piperazinediylbis(3,1-propanediylimino)]bis[4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-amino-4-(3,4-dimethoxyphenyl)-1H-pyrrole-2,5-dione;
3-[(5-aminopentyl)amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-[[5-[(2-aminoethyl)amino]pentyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-[(2-aminoethyl)amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-[(6-aminohexyl)amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-[(7-aminoheptyl)amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-[[2-[(2-aminoethyl)amino]ethyl]amino]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
Benzenepropanamide, .alpha.-amino-N-[5-[[2,5-dihydro-4-(1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]amino]pentyl]-, (S)-;
Pentanoic acid, 4-amino-5-[[5-[[2,5-dihydro-4-(1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]amino]pentyl]amino]-5-oxo-, (S)-;
Pentanamide, 2-amino-5-[(aminoiminomethyl)amino]-N-[2-[[5-[[2,5-dihydro-4-(1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]amino]pentyl]amino]ethyl]-, (S)-;
Benzenepropanamide, .alpha.-amino-N-[2-[[5-[[2,5-dihydro-4-(1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]amino]pentyl]amino]ethyl]-, (S)-;
Butanamide, 4-[(aminoiminomethyl)amino]-N-[5-[[2,5-dihydro-4-(1H-indol-3-yl)-2,5-dioxo-1H-pyrrol-3-yl]amino]pentyl]-, (S)-;
3-amino-1,4-diphenyl-1H-pyrrole-2,5-dione;
3-(4-methylphenyl)-1-phenyl-4-[(phenylmethyl)amino]-1H-pyrrole-2,5-dione;
3-amino-4-(4-methylphenyl)-1-phenyl-1H-pyrrole-2,5-dione;
3-amino-1-methyl-4-p-tolyl-1H-pyrrole-2,5-dione;
3-(2-diethylamino-ethylamino)-4-phenyl-pyrrole-2,5-dione;
3-[butyl-(2-diethylamino-ethyl)-amino]-4-phenyl-pyrrole-2,5-dione;
3-[benzyl-(2-dimethylamino-ethyl)-amino]-4-phenyl-pyrrole-2,5-dione;
3-[benzyl-(2-dimethylamino-ethyl)-amino]-1-methyl-4-phenyl-pyrrole-2,5-dione;
3-[benzyl-(2-dimethylamino-ethyl)-amino]-4-(4-chloro-phenyl)-pyrrole-2,5-dione;
3-[benzyl-(2-diethylamino-ethyl)-amino]-4-phenyl-pyrrole-2,5-dione;
3-[benzyl-(2-dimethylamino-ethyl)-amino]-4-(3-methoxy-phenyl)-pyrrole-2,5-dione;
3-(4-chloro-phenyl)-4-[2-(4-methyl-piperazin-1-yl)-ethylamino]-pyrrole-2,5-dione;
3-[2-(4-methyl-piperazin-1-yl)-ethylamino]-4-phenyl-pyrrole-2,5-dione;
3-phenyl-4-(diethylamino)-pyrrole-2,5-dione;

3-phenyl-4-(benzylamino)-pyrrole-2,5-dione;
1-methyl-3-phenyl-4-(2-diethylaminoethylamino)-pyrrole-2,5-dione, and;
1-allyl-3-phenyl-4-(2-dimethylaminoethylamino)-pyrrole-2,5-dione.

Suitably $R^{2'}$ is indolyl, phenyl or phenyl substituted with one or more, suitably up to three, substituents selected from the list consisting of: halo, haloalkyl, alkoxy, nitro, alkyl and alkoxy.

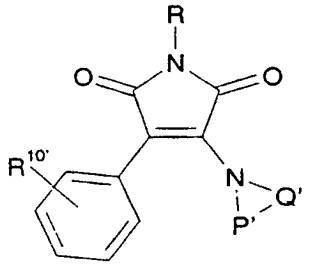
Examples of $R^{2'}$ include phenyl, indol-3-yl, 2-methoxyphenyl, 3-fluorophenyl, 3-nitrophenyl, 4-chlorophenyl, 4-iodophenyl, 4-(trifluoromethyl)phenyl and 2,3-difluorophenyl.

Suitably $R^{3'}$ represents hydrogen, C_{1-6} alkyl, cyclohexyl, phenyl, fluorenyl, C_{1-2} alkylphenyl, C_{1-6}alkoxyC_{1-2}alkyl or a substituted or unsubstituted single or a single or fused ring heterocyclyl group having 5 or 6 ring atoms and up to 3 hetero atoms in each ring, such as oxazolyl, benzofuranyl, dibenzofuranyl, pyridinyl, quinolinyl, pyrimidinyl.

Examples of $R^{3'}$ include hydrogen, ethyl, cyclohexyl, phenyl, fluoren-2-yl, benzyl, phenyl$(CH_2)_2$-, $MeO(CH_2)_2$-, 4-methyloxazol-2-yl, 2-acetylbenzofuran-5-yl, dibenzofuran-2-yl, dibenzofuran-3-yl, 2-methylpyridin-3-yl 2,6-dimethylpyridin-3-yl, 2-chloropyridin-5-yl, quinolin-3-yl, pyrimidin-2-yl.

It is considered that the compounds of formula (ID') are novel. Accordingly , the present invention also provides a compound of the above defined formula (ID') or a derivative thereof.

There is a subgroup of compounds falling wholly within formula (I) being of formula (IE):



(IE)

wherein R is as defined in relation to formula (I);

$R^{10'}$ represents hydrogen or one or more, suitably up to three, substituents selected from the list consisting of: alkoxy, halo, and nitro;

P'-Q' represents $-(CH_2)_aO(CH_2)_b$-, $-(CH_2)_aS(CH_2)_b$-, $-(CH_2)_c$-, $-(CH_2)_dCH(G)(CH_2)_e$-, $-(CH_2)_aN(ZZ)(CH_2)_b$ -,where a, b, d, and e are independently 1 to 4, c is 1 to 6, ZZ is hydrogen, alkyl, aryl, or alkylcarbonyl, and G is alkyl, amido, hydroxyalkyl, aralkyl, or hydroxy.

There is a subgroup of compounds within formula (IE) of formula (IE') wherein R, $R^{10'}$, and P'-Q' are as defined in relation to formula (IE) with the proviso that formula (IE') does not include:

3-phenyl-4-piperidin-1-yl-pyrrole-2,5-dione;
3-(4-methylpiperazin-1-yl)-4-phenyl-pyrrole-2,5-dione;
3-(4-ethylpiperazin-1-yl)-4-phenyl-pyrrole-2,5-dione;
3-(4-chlorophenyl)-4-(4-methyl-piperazin-1-yl)-pyrrole-2,5-dione;
3-(4-methylphenyl)-4-(4-morpholinyl)-1-phenyl-1H-pyrrole-2,5-dione
3-phenyl-4-(4-methylpiperazino)-pyrrole-2,5-dione;
3-phenyl-4-(4-phenylpiperazino)-pyrrole-2,5-dione;
1-methyl-3-phenyl-4-(4-phenylpiperazino)-pyrrole-2,5-dione;
1-ethyl-3-phenyl-4-(4-chlorophenylpiperazino)-pyrrole-2,5-dione;
1-allyl-3-phenyl-4-(4-methylpiperazino)-pyrrole-2,5-dione, and;
1,3-diphenyl-4-piperidino-pyrrole-2,5-dione.

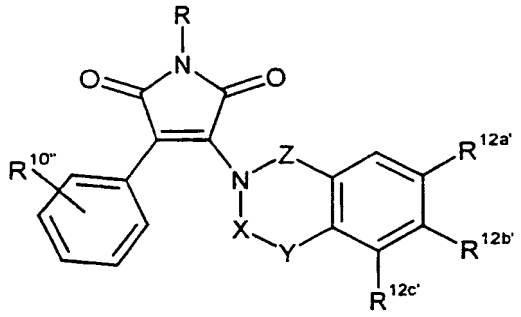
Suitably, $R^{10'}$ is methoxy, chloro, or nitro.

Examples of $R^{10'}$ include 4-methoxy, 4-chloro, 2,4-dichloro, and 3-nitro.

Examples of -P'-Q'- include $-(CH_2)_4-$, $-(CH_2)_2O(CH_2)_2-$, $-(CH_2)_3CH(Me)CH_2-$, $-(CH_2)_3CH(CONH_2)CH_2-$, $-(CH_2)_3CH(CH_2OH)CH_2-$, $-(CH_2)_2CH(CH_2Ph)(CH_2)_2-$, $-(CH_2)_2CH(OH)(CH_2)_2-$, $-(CH_2)_5-$, and $-(CH_2)S(CH_2)_2-$

It is considered that the compounds of formula (IE') are novel. Accordingly , the present invention also provides a compound of the above defined formula (IE') or a derivative thereof.

There is a subgroup of compounds falling wholly within formula (I) being of formula (IF):



(IF)

wherein R is as defined in relation to formula (I);

R10" is one or more, suitably up to three, substituents selected from the list consisting of perfluoroalkyl, halo, nitro, alkoxy, arylcarbonyl, alkyl;

Z is a bond or an alkylene chain;

-X-Y- is $-CH=N$, $-(CH_2)_t-$, $-(CH_2)_uCH(U)-$, $-(U)CH(CH_2)_u-$, $-CH=CH-$, $-(CH_2)_vC(alkyl)_2-$, $-C(O)C(alkyl)_2-$, $-C(O)O-$, where t, u, and v are independently 1 to 4, and U is alkyl, carboxy, alkoxycarbonyl, hydroxyalkyl, and amido;

$R^{12a'}$, $R^{12b'}$, and $R^{12c'}$ are each independently hydrogen, nitro, alkoxy, 4-ethylpiperazin-1-yl, 4-BOC-piperazin-1-yl, 4-methyl-piperazin-1-yl, 4-methyl-piperazin-1-yl, halo, alkyl, piperazin-1-yl, perfluoroalkyl, and alkylsulphonylamino.

Suitably, Z is a bond or a C_{1-2} alkylene chain.

Examples of Z include a bond, methylene or ethylene.

Examples of -X-Y- are –CH=N-, -$(CH_2)_2$-, -CH(Me)CH_2-, -CH=CH-, -CH(CO_2H)CH_2-, -CH(CO_2Me)CH_2-, -$(CH_2)_3$-, -CH(CH_2OH)CH_2-, -CH_2CH(CH_2OH)-, -CH_2CH(Me)-, -CH_2C(Me)$_2$-, -CH($CONH_2$)CH_2-, -C(O)C(Me)$_2$-, and -C(O)O-

Examples of $R^{12a'}$, $R^{12b'}$, and $R^{12c'}$ include hydrogen, nitro, fluoro, methoxy, 4-ethylpiperazin-1-yl, 4-BOC-piperazin-1-yl, 4-methyl-piperazin-1-yl, 4-methyl-piperazin-1-yl, chloro, bromo, trifluoromethyl, and methanesulphonylamino.

Preferably, Z is a bond.

Preferably, -X-Y- is –$(CH_2)_2$- or –CH(CH_2OH)CH_2-, -CH(Me)CH_2-, -CH_2CH(Me)-, or –CH_2C(Me)$_2$-.

Preferably, $R^{12b'}$ is fluorine.

Preferably, $R^{12a'}$ is fluorine.

Most preferably, $R^{10''}$ is 2-Br, 2-Cl, 2-F, 2-OMe, 3-Cl, 3-F, 3-Me, 4-Br, 4-Cl, 4-I, 2,3-di-F, 2,5-di-F, 2,6-di-F, 3,4-di-F, 3,5-di-F, 2,3,5-tri-F, 2,4-di-Cl, 3,5-di-Me;

Z is a bond;

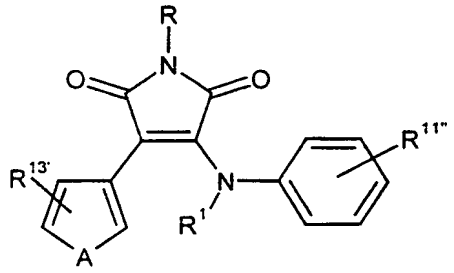
-X-Y- is –$(CH_2)_2$- or –CH(CH_2OH)CH_2-, -CH(Me)CH_2-, -CH_2CH(Me)-, or –CH_2C(Me)$_2$-,

$R^{12b'}$ is fluorine; and

$R^{12a'}$ is fluorine.

It is considered that the compounds of formula (IF) are novel. Accordingly , the present invention also provides a compound of the above defined formula (IF) or a derivative thereof.

There is a subgroup of compounds falling wholly within formula (I) being of formula (IG):



(IG)

wherein R and R^1 are as defined in relation to formula (I);

A is N(alkyl), oxygen, or sulphur.

Examples of A are N(methyl), oxygen, and sulphur.

Preferably, A is sulphur.

$R^{11''}$ is one or more, suitably up to three, substituents selected from the group consisting of hydrogen, halo, alkyl, alkylthio, -S-CH=N-, phenoxy, -$(CH_2)_w$-, hydroxy,

carboxy, $-O(CH_2)_xO-$, hydroxyalkyl, and alkylaminosulphonylalkyl, where w and x are independently 1 to 4.

Examples of $R^{11''}$ are hydrogen, bromo, methyl, methylthio, chloro, -S-CH=N-, phenoxy, $-(CH_2)_3-$, hydroxy, carboxy, $-O(CH_2)O-$, fluoro, hydroxymethyl, and $MeNHSO_2CH_2-$.

Preferably, $R^{11''}$ is 3-Br, 4-Me, 4-SMe, 3-Br-4-Me, 3-Cl, 3,4-[S-CH=N]-, 3-OPh, 3,4-$[(CH_2)_3]$-, 3-SMe, hydrogen, 3,5-diBr-4-OH, 3,5-diCl-4-OH, $3-CO_2H-4-Cl$, 3,4-$[-OCH_2O]$-, 3-Cl-4-OH, 3,5-diF, $3-CH_2OH$, 3-OH, or $4-CH_2SO_2NHMe$.

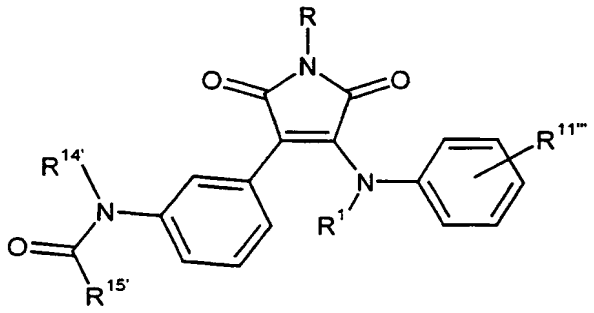
$R^{13'}$ is one or more, suitably up to two, substituents selected from the group consisting of $-(CH=CH)_2-$ and hydrogen.

Examples of $R^{13'}$ include 4,5-$[(CH=CH)_2]$- and hydrogen.

Preferably, $R^{13'}$ is hydrogen.

It is considered that the compounds of formula (IG) are novel. Accordingly , the present invention also provides a compound of the above defined formula (IG) or a derivative thereof.

There is a subgroup of compounds falling wholly within formula (I) being of formula (IH):



(IH)

wherein R and R^1 are as defined in relation to formula (I);

$R^{11'''}$ is $-[(CH_2)_{aa}]-$, where aa is 1 to 4;

$R^{14'}$ is hydrogen;

$R^{15'}$ is alkyl, unsubstituted or substituted phenylamino, unsubstituted or substituted phenylalkylamino, cyclohexylamino, alkenylamino, phenyl, benzyl, styryl, or alkylamino.

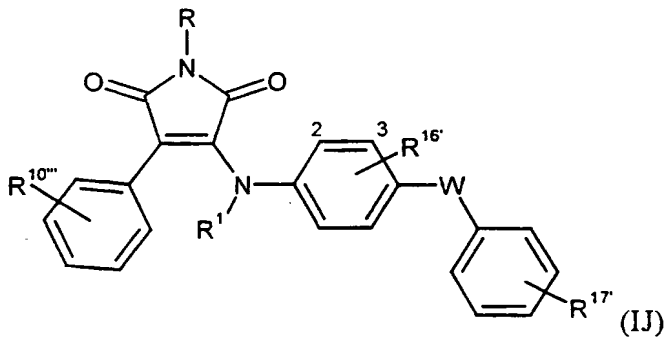
Examples of $R^{11'''}$ include 3,4-$[(CH_2)_3]$.

Suitably, $R^{15'}$ is C_{1-6}alkyl, (halophenyl)amino, phenylalkylamino, cyclohexylamino, propenylamino, phenyl, benzyl, styryl, propyl, ethylamino, or (methoxyphenyl)amino.

Examples of $R^{15'}$ include methyl, (3-fluorophenyl)amino, phenylethylamino, cyclohexylamino, propenylamino, phenyl, benzyl, *trans*-styryl, *n*-propyl, ethylamino, and (3-methoxyphenyl)amino.

It is considered that the compounds of formula (IH) are novel. Accordingly , the present invention also provides a compound of the above defined formula (IH) or a derivative thereof.

There is a subgroup of compounds falling wholly within formula (I) being of formula (IJ):



(IJ)

wherein R and R^1 are as defined in relation to formula (I);

$R^{10'''}$ represents one or more, suitably up to three, substituents independently selected from alkoxy or halo;

$R^{16'}$ represents one or more, suitably up to three, substituents independently selected from hydrogen, carboxy, alkoxycarbonyl, or alkylaminocarbonyl;

$R^{17'}$ represents one or more, suitably up to three, substituents independently selected from carboxy, alkoxycarbonyl, halo, alkylaminocarbonyl, nitro, or hydrogen;

W is sulphur, oxygen, or substituted or unsubstituted NH.

Suitably, W is sulphur or oxygen. Favourably, W is sulphur.

Suitably, $R^{10'''}$ is C_{1-6}alkoxy, chloro, or fluoro.

Examples of $R^{10'''}$ are methoxy, 4-chloro, 2-chloro, and 2,3-difluoro.

Favourably, $R^{10'''}$ is 2,3-difluoro.

Suitably, $R^{16'}$ is hydrogen, carboxy, C_{1-6}alkoxycarbonyl, or C_{1-6}alkylaminocarbonyl.

Examples of $R^{16'}$ are carboxy, hydrogen, ethoxycarbonyl, methoxycarbonyl, and methylaminocarbonyl.

Favourably, $R^{16'}$ is hydrogen.

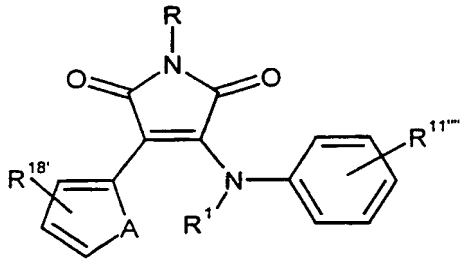
Suitably, $R^{17'}$ is carboxy, C_{1-6}alkoxycarbonyl, halo, C_{1-6}alkylaminocarbonyl, nitro, or hydrogen;

Examples of $R^{17'}$ are 2-carboxy, 3-carboxy, 4-carboxy, 4-chloro, 2-methylaminocarbonyl, 4-nitro, hydrogen, and 2-ethoxycarbonyl.

Favourably, $R^{17'}$ is 3-carboxy.

It is considered that the compounds of formula (IJ) are novel. Accordingly , the present invention also provides a compound of the above defined formula (IJ) or a derivative thereof.

There is a subgroup of compounds falling wholly within formula (I) being of formula (IK):



(IK)

wherein R and R^1 are as defined in relation to formula (I);

$R^{11''''}$ represents one or more, suitably up to three, substituents independently selected from halo and hydroxy;

$R^{18'}$ represents one or more, suitably up to three, substituents independently selected from hydrogen, alkyl, and $-(CH=CH)_2-$;

A is sulphur.

Suitably, $R^{11''''}$ is chloro or hydroxy.

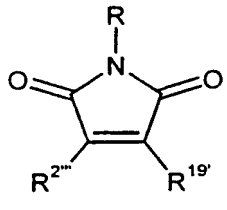
Examples of $R^{11''''}$ are 3-chloro and 3,5-dichloro-4-hydroxy.

Suitably, $R^{18'}$ is hydrogen, C_{1-6}alkyl, or $-(CH=CH)_2-$.

Examples of $R^{18'}$ include hydrogen, methyl, and 3-methyl-4,5-[$(CH=CH)_2$]-.

It is considered that the compounds of formula (IK) are novel. Accordingly , the present invention also provides a compound of the above defined formula (IK) or a derivative thereof.

There is a subgroup of compounds falling wholly within formula (I) being of formula (IL):



(IL)

wherein R is as defined in relation to formula (I);

$R^{2'''}$ is unsubstituted or substituted heterocyclyl or unsubstituted or substituted aryl;

$R^{19'}$ is unsubstituted or substituted heterocyclyl, or a quaternised salt thereof.

There is a subgroup of compounds within formula (IL) of formula (IL') wherein R, $R^{2'''}$, and $R^{19'}$ are as defined in relation to formula (IL) with the proviso that (IL') does not include the following compounds, hereinafter referred to as List L':

3-indol-1-yl-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione:
1-(1-methyl-2,5-dioxo-4-phenylamino-2,5-dihydro-1H-pyrrol-3-yl)-pyridinium chloride;
1-1-(4-methyl-pentyl)-2,5-dioxo-4-phenylamino-2,5-dihydro-1H-pyrrol-3-yl)-pyridinium chloride;
1-(1-dodecyl-2,5-dioxo-4-phenylamino-2,5-dihydro-1H-pyrrol-3-yl)-pyridinium chloride;
3-[2,5-dihydro-4-(1H-imidazol-1-yl)-1-methyl-2,5-dioxo-1H-pyrrol-3-yl]-1H-indole-1-carboxylic acid, 1,1-dimethylethyl ester;
3-(1H-imidazo[4,5-b]pyridin-l-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione:
3-(1H-indol-3-yl)-1-methyl-4-(1H-pyrrolo[2,3-b]pyridin-1-yl)-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-(1-piperidinyl)-1H-pyrrole-2,5-dione;
3-[4-(diphenylmethyl)-1-piperazinyl]-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-benzimidazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-benzotriazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-imidazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-indol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-indazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-[3-[(dimethylamino)methyl]-1H-indol-1-yl]-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-benzimidazol-1-yl)-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione;
3-(1H-indol-1-yl)-4-(1-methyl-1H-indol-3-yl)-1H-pyrrole-2,5-dione, and;
3-(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)-4-(4-morpholinyl)-1H-pyrrole-2,5-dione.

Suitably, $R^{2'''}$ is thienyl, phenyl, or phenyl substituted with one or more halogen groups.

Examples of $R^{2'''}$ include phenyl, 3-thienyl, 2-thienyl, 4-chlorophenyl, and 2,4-dichlorophenyl.

Favourably, $R^{2'''}$ is phenyl, 3-thienyl, 4-chlorophenyl, or 2,4-dichlorophenyl.

Suitably, $R^{19'}$ is indolinyl, pyridinium halide, azabicyclooctanyl, or triazaspirodecanonyl.

Examples of $R^{19'}$ include indolin-1-yl, 3-amino-1-pyridinium chloride, 2-methylindolin-1-yl, 1,3,3-trimethyl-6-azabicyclo[3.2.1]octan-6-yl, and 1-phenyl-1,3,8-triazaspiro-[4,5]-decan-4-one-8-yl.

Favourably, $R^{19'}$ is indolin-1-yl, or 2-methylindolin-1-yl.

It is considered that the compounds of formula (IL') are novel. Accordingly , the present invention also provides a compound of the above defined formula (IL') or a derivative thereof.

Certain of the compounds of formula (I) may contain at least one chiral carbon, and hence they may exist in one or more stereoisomeric forms. The present invention encompasses all of the isomeric forms of the compounds of formula (I) whether as individual isomers or as mixtures of isomers, including racemates.

Alkyl groups referred to herein, including those forming part of other groups, include straight or branched chain alkyl groups containing up to six carbon atoms, said carbon atoms being optionally substituted with up to five, suitably up to three, groups selected from the list consisting of aryl, heterocyclyl, alkylthio, alkenylthio, alkynylthio, arylthio, heterocyclylthio, alkoxy, arylalkoxy, arylalkylthio, amino, mono- or di-alkylamino, cycloalkyl, cycloalkenyl, carboxy and esters thereof, phosphonic acid and esters thereof, mono- or dialkylaminosulphonyl, aminosulphonyl, cyano, alkylcarbonylamino, arylcarbonylamino, hydroxy, and halogen.

Alkenyl and alkynyl groups referred to herein include straight and branched chain alkenyl groups containing from two to six carbon atoms, said carbon atoms being optionally substituted with up to five, suitably up to three, groups including those substituents described hereinbefore for the alkyl group.

Cycloalkyl and cycloalkenyl groups referred to herein include groups having between three and eight ring carbon atoms, which carbon atoms are optionally substituted with up to five, suitably up to three, groups including those substituents described hereinbefore for the alkyl group.

When used herein the term "aryl" includes phenyl and biphenyl groups, for example naphthyl, especially phenyl.

Suitably optional substituents for any aryl group include up to three substituents selected from the list consisting of halo, alkyl, alkenyl, substituted alkenyl, arylalkyl, alkoxy, alkoxyalkyl, haloalkyl, haloalkyloxy, hydroxy, hydroxyalkyl, nitro, amino, cyano, cyanoalkyl , mono- and di-N-alkylamino, acyl, acylamino, N-alkylacylamino, acyloxy, carboxy, carboxyalkyl, carboxyalkylcarbonyl, carboxyalkenyl, ketoalkylester, carbamoyl, carbamoylalkyl, mono- and di-N-alkylcarbamoyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy, arylthio, aralkyloxy, aryloxycarbonyl, ureido, guanidino, morpholino, adamantyl, oxazolyl, aminosulphonyl, alkylaminosulphonyl, alkylthio, haloalkylthio, alkylsulphinyl, alkylsulphonyl, cycloalkyl, heterocyclyl, heterocyclylalkyl, trityl, substituted trityl, mono- or bis-alkylphosphonate or mono- or bis-alkylphosphonateC_{1-6}alkyl or any two adjacent substituents on the phenyl ring together with the carbon atoms to which they are attached form a carbocyclic ring or a heterocyclic ring.

When used herein the terms "heterocyclyl" and "heterocyclic" suitably include, unless otherwise defined, aromatic and non-aromatic, single and fused, rings suitably containing up to four heteroatoms in each ring, each of which is selected from oxygen, nitrogen and sulphur, which rings, may be unsubstituted or substituted by, for example, up to three substituents. Each ring suitably has from 4 to 7, preferably 5 or 6, ring atoms. A fused heterocyclic ring system may include carbocyclic rings and need include only one heterocyclic ring.

Substituents for any heterocyclyl or heterocyclic group are suitably selected from halogen, alkyl, arylalkyl, alkoxy, alkoxyalkyl, haloalkyl, hydroxy, amino, mono- and di-N-alkyl-amino, acylamino, carboxy salts, carboxy esters, carbamoyl, mono- and di-N-alkylcarbonyl, aryloxycarbonyl, alkoxycarbonylalkyl, aryl, oxy groups, ureido, guanidino, sulphonylamino, aminosulphonyl, alkylthio, alkylsulphinyl, alkylsulphonyl, heterocyclyl and heterocyclylalkyl.

When used herein 'halo' includes iodo, bromo, chloro or fluoro, especially chloro or fluoro.

Suitable derivatives of the compounds of the invention are pharmaceutically acceptable derivatives.

Suitable derivatives of the compounds of the invention include salts and solvates.

Suitable pharmaceutically acceptable derivatives include pharmaceutically acceptable salts and pharmaceutically acceptable solvates.

Suitable pharmaceutically acceptable salts include metal salts, such as for example aluminium, alkali metal salts such as lithium, sodium or potassium, alkaline earth metal salts such as calcium or magnesium and ammonium or substituted ammonium salts, for example those with lower alkylamines such as triethylamine, hydroxy alkylamines such as 2-hydroxyethylamine, bis-(2-hydroxyethyl)-amine or tri-(2-hydroxyethyl)-amine, cycloalkylamines such as bicyclohexylamine, or with procaine, dibenzylpiperidine, N-benzyl-β-phenethylamine, dehydroabietylamine, N,N'-bisdehydroabietylamine, glucamine, N-methylglucamine or bases of the pyridine type such as pyridine, collidine, quinine or quinoline.

Suitable pharmaceutically acceptable salts also includes pharmaceutically acceptable acid addition salts, such as those provided by pharmaceutically acceptable inorganic acids or organic acids.

Suitable pharmaceutically acceptable acid addition salts provided by pharmaceutically acceptable inorganic acids includes the sulphate, nitrate, phosphate, borate, hydrochloride and hydrobromide and hydroiodide.

Suitable pharmaceutically acceptable acid addition salts provided by pharmaceutically acceptable organic acids includes the acetate, tartrate, maleate, fumarate, malonate, citrate, succinate, lactate, oxalate, benzoate, ascorbate, methanesulphonate, α-keto glutarate and α-glycerophosphate.

Suitable pharmaceutically acceptable solvates include hydrates.

For the avoidance of doubt when used herein the term "diabetes " includes diabetes mellitus, especially Type 2 diabetes, and conditions associated with diabetes mellitus.

The term 'conditions associated with diabetes' includes those conditions associated with the pre-diabetic state, conditions associated with diabetes mellitus itself and complications associated with diabetes mellitus.

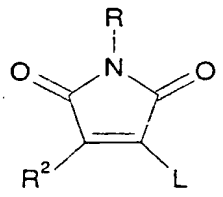
The term 'conditions associated with the pre-diabetic state' includes conditions such as insulin resistance, impaired glucose tolerance and hyperinsulinaemia.

The term 'conditions associated with diabetes mellitus itself' include hyperglycaemia, insulin resistance and obesity. Further conditions associated with diabetes mellitus itself include hypertension and cardiovascular disease, especially atherosclerosis and conditions associated with insulin resistance. Conditions associated with insulin resistance include polycystic ovarian syndrome and steroid induced insulin resistance.

The term 'complications associated with diabetes mellitus' includes renal disease, especially renal disease associated with Type II diabetes, neuropathy and retinopathy.

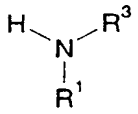
glomerular sclerosis, nephrotic syndrome, hypertensive nephrosclerosis and end stage renal disease.

A further aspect of the invention provides a process for the preparation of a compound of the invention, which process comprises reaction of a compound of formula (II):



(II)

wherein R and R^2 are as defined in formula (I) and L is a leaving group, with a compound of formula (III):



(III)

wherein R^1 and R^3 are as defined in formula (I); and thereafter, if required, carrying out one or more of the following optional steps:

(i) converting a compound of formula (I) to a further compound of formula (I);

(ii) removing any necessary protecting group;

(iii) preparing an appropriate derivative of the compound so formed.

Examples of suitable leaving groups, L, are chloro, bromo, triflate, and hydroxy.

The reaction between the compounds of formulae (II) and (III) is carried out in any suitable solvent, for example 1-methyl-2-pyrrolidinone, tetrahydrofuran, 0.880 ammonia, or methanol, under conventional amination conditions at any temperature providing a suitable rate of formation of the required product, generally an elevated temperature, over a suitable reaction time.

Suitable reaction temperatures include those in the range of 60°C to 220°C and, as appropriate, the reflux temperature of the solvent. When the compound of formula (III) is a weak nucleophile, then the reaction may be assisted by, for example, using temperatures at the upper end of this range, generating the anion of the compound of formula (III) *in situ* using, for example, sodium hydride, or by using a basic catalyst such as triethylamine. Conventional methods of heating also include the use of microwave heating devices, for example a microwave reactor, such as a 100 watt reactor.

The reaction products are isolated using conventional methods. Typically, the reaction mixture is cooled, the residue acidified and the products extracted using solvent extraction, suitably using an organic solvent.

The reaction products are purified by conventional methods, such as chromatography and trituration.

Crystalline product may be obtained by standard methods.

Crystalline product may be obtained by standard methods.

In a preferred aspect, a solution of the compound of formula (II) and a compound of formula (III) in methanol is heated to reflux from between 1 to 4 days, then cooled and concentrated. The residue is then acidified with hydrochloric acid, and extracted with ethyl acetate. The organic extracts are then washed with water, brine, dried with anhydrous magnesium sulphate, and the solvent is removed. The product is then purified by standard methods such as trituration or chromatography, on silica gel, to afford the desired compound.

The above mentioned conversion of a compound of formula (I) into another compound of formula (I) includes any conversion which may be effected using conventional procedures, but in particular the said conversions include any combination of:

(i) converting one group R into another group R;

(ii) converting one group R^3 into another group R^3;

(iii) converting one group R^{10} into another group R^{10}, and;

(iv) converting one group R^{11} into another group R^{11}.

The above mentioned conversions (i) to (iv) may be carried out using any appropriate method under conditions determined by the particular groups chosen.

Thus, suitable conversions of one group R into another group R, as in conversion (i), include:

(a) converting a group R which represents hydrogen into a group R which represents an alkyl or arylalkyl group; such conversion may be carried out using an appropriate conventional alkylation procedure, for example treating an appropriately protected compound of formula (I) with an alkylating agent; and

(b) converting a group R which represents an alkyl group into a group R where R represents hydrogen; such conversion may be carried out using an appropriate dealkylation procedure, for example treating an appropriately protected compound of formula (I) with aqueous base followed by ammonium hydroxide.

Suitable conversions of one group NR^1R^3 into another group NR^1R^3, as in conversion (ii), include:

converting a group NR^1R^3 which represents arylamino into another group NR^1R^3 which represents alkylamino; such conversion may be carried out using an appropriate conventional procedure, for example treating an appropriately protected compound of formula (I) with an alkylamine.

Suitable conversions of one group R^{10} into another group R^{10}, as in conversion (iii), include:

(a) converting a group R^{10} which represents nitro into a group R^{10} which represents amino, such conversion may be carried out using a conventional reduction procedure, for example hydrogenating an appropriately protected compound of formula (I);

(b) converting a group R^{10} which represents nitro into a group R^{10} which represents acetylamino, such conversion may be carried out using an appropriate conventional reductive acylation procedure, for example hydrogenating an appropriately protected

compound of formula (I) followed by acylation of the resultant amino group with an acylating agent;

(c) converting a group R^{10} which represents amino into a group R^{10} which represents a substituted urea, such conversion may be carried out using an appropriate conventional amidation procedure, for example treating an appropriately protected compound of formula (I) with an appropriately substituted isocyanate;

(d) converting a group R^{10} which represents amino into a group R^{10} which represents acylamino, such conversion may be carried out using an appropriate conventional acylation procedure, for example treating an appropriately protected compound of formula (I) with an acylating agent, or treating an appropriately protected compound of formula (I) with a suitable carboxylic acid in the presence of activating agents such as a mixture of 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide, and;

(e) converting a group R^{10} which represents iodo into a group R^{10} which represents alkoxycarbonyl, such conversion may be carried out using an appropriate procedure, for example treating an appropriately protected compound of formula (I) with carbon monoxide and methanol in the presence of a palladium (0) complex.

Suitable conversions of one group R^{11} into another group R^{11}, as in conversion (iv), include:

(a) converting a group R^{11} which represents a t-BOC-protected amino group into a group R^{11} which represents amino, such conversion may be carried out using an appropriate conventional deprotection procedure, for example deprotecting a t-BOC-protected compound of formula (I) with trifluoroacetic acid;

(b) converting a group R^{11} which represents a carboxylic acid group into a group R^{11} which represents an amide group, such conversion may be carried out using an appropriate conventional procedure, for example treating an appropriately protected compound of formula (I) with an amine in the presence of suitable activating agents such as a mixture of 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide; and

(c) converting a group R^{11} which represents alkoxycarbonyl into a group R^{11} which represents carbamoyl, such conversion may be carried out using an appropriate conventional procedure, for example treating an appropriately protected compound of formula (I) with methanolic ammonia solution followed by aqueous ammonia.

The above mentioned conversions may as appropriate be carried out on any of the intermediate compounds mentioned herein.

Suitable protecting groups in any of the above mentioned reactions are those used conventionally in the art The methods of formation and removal of such protecting groups are those conventional methods appropriate to the molecule being protected. Thus for example a benzyloxy group may be prepared by treatment of the appropriate compound with a benzyl halide, such as benzyl bromide, and thereafter, if required, the benzyl group may be conveniently removed using catalytic hydrogenation or a mild ether cleavage reagent such as trimethylsilyl iodide or boron tribromide.

Where appropriate individual isomeric forms of the compounds of formula (I) may be prepared as individual isomers using conventional procedures.

The absolute stereochemistry of compounds may be determined using conventional methods, such as X-ray crystallography.

The derivatives of the compounds of formula (I), including salts and/or solvates, may be prepared and isolated according to conventional procedures.

The compounds of formula (II) are known compounds or they may be prepared using methods analogous to those used to prepare such compounds such as those described in International Patent Application, Publication Number WO97/34890 and Wiley, R.H. and Slaymaker, S.C. J. Am. Chem. Soc. (80) 1385 (1958). The compounds of formula (II) may be inter-converted in an analogous manner to the above mentioned inter-conversions of the compounds of formula (I).

The compounds of formula (III) are either commercially available, or are reported in the chemical literature, or are prepared by analogy with known conventional literature procedures, for example those disclosed in *Chem. Ber.*, 1892, *25*, 2977, *J. Amer. Chem. Soc.*, 1948, *70*, 4174-4177, *Synthesis* 1977, 859, *J. Med. Chem.*, 1994, *37*, 3956, *Synthesis* 1994, 1413, and *Tetrahedron*, 1991, *47*, 2661, or in standard reference texts of synthetic methodology such as J. March, Advanced Organic Chemistry, 3rd Edition (1985), Wiley Interscience.

As stated above, the compounds of formula (I), or pharmaceutically acceptable derivatives thereof, are indicated to be useful as inhibitors of glycogen synthase kinase-3.

Thus the present invention further provides a compound of formula (I), or a pharmaceutically acceptable derivative thereof, for use as an inhibitor of glycogen synthase kinase-3, and especially for use in the treatment of conditions associated with a need for the inhibition of glycogen synthase kinase-3, such as diabetes, especially Type 2 diabetes, dementias, such as Alzheimer's disease and manic depression.

The present invention also provides the use of a compound of formula (I), or a pharmaceutically acceptable derivative thereof, for the manufacture of a medicament for the treatment of conditions associated with a need for the inhibition of glycogen synthase kinase-3, such as diabetes, especially Type 2 diabetes, dementias, such as Alzheimer's disease and manic depression.

As indicated above, formula (I) comprises a sub-group of compounds of formula (IA). In a further aspect of this invention, there is provided a compound of formula (IA), or a pharmaceutically acceptable derivative thereof, for use as an active therapeutic substance.

Accordingly, the invention also provides a pharmaceutical composition which comprises a compound of formula (IA), or a pharmaceutically acceptable derivative thereof, and a pharmaceutically acceptable carrier.

Preferably, the compounds of formula (I), or pharmaceutically acceptable derivatives thereof are administered as pharmaceutically acceptable compositions.

As indicated above it is considered that GSK-3 inhibitors *per se* are potentially useful in the treatment and/or prophylaxis of mood disorders, such as schizophrenia,

neurotraumatic diseases, such as acute stroke, and for the treatment and/or prophylaxis of cancer and hair loss.

Accordingly, in a further aspect the invention provides a method for the treatment and/or prophylaxis of mood disorders, such as schizophrenia, in a mammal, such as a human, which method comprises the administration of a pharmaceutically acceptable amount of a GSK-3 inhibitor.

The invention also provides a method for the treatment and/or prophylaxis of neurotraumatic diseases in a mammal, such as a human, which method comprises the administration of a pharmaceutically acceptable amount of a GSK-3 inhibitor.

Neurotraumatic diseases include both open or penetrating head trauma, such as caused by surgery, or a closed head trauma injury, such as caused by an injury to the head region ischaemic stroke, including acute stroke, particularly to the brain area, transient ischaemic attacks following coronary by-pass and cognitive decline following other transient ischaemic conditions.

Further provided is a method for the treatment and/or prophylaxis of cancer, in a mammal, such as a human, which method comprises the administration of a pharmaceutically acceptable amount of a GSK-3 inhibitor.

In addition there is provided a method for the treatment and/or prophylaxis of hair-loss, in a mammal, such as a human, which method comprises the administration of a pharmaceutically acceptable amount of a GSK-3 inhibitor.

Thus, the invention also provides the use of a GSK-3 inhibitor for the manufacture of a medicament for the treatment and/or prophylaxis of mood disorders, schizophrenia, neurotraumatic diseases, cancer or hair-loss.

A suitable GSK-3 inhibitor is a compound of formula (I) or a pharmaceutically acceptable derivative thereof.

The active compounds are usually administered as the sole medicament agent but they may be administered in combination with other medicament agents as dictated by the severity and type of disease being treated. For example in the treatment of diabetes, especially Type 2 diabetes, a compound of formula (I), or a pharmaceutically acceptable derivative thereof, may be used in combination with other medicament agents, especially antidiabetic agents such as insulin secretagogues, especially sulphonylureas, insulin sensitisers, especially glitazone insulin sensitisers (for example thiazolidinediones), or with biguanides or alpha glucosidase inhibitors or the compound of formula (I), or a pharmaceutically acceptable derivative thereof, may be administered in combination with insulin.

The said combination comprises co-administration of a compound of formula (I), or a pharmaceutically acceptable derivative thereof, and an additional medicament agent or the sequential administration of a compound of formula (I), or a pharmaceutically acceptable derivative thereof, and the additional medicament agent.

Co-administration includes administration of a pharmaceutical composition which contains both a compound of formula (I), or a pharmaceutically acceptable derivative thereof, and the additional medicament agent or the essentially simultaneous

administration of separate pharmaceutical compositions of a compound of formula (I), or a pharmaceutically acceptable derivative thereof, and the additional medicament agent.

The compositions of the invention are preferably adapted for oral administration. However, they may be adapted for other modes of administration.

The compositions may be in the form of tablets, capsules, powders, granules, lozenges, suppositories, reconstitutable powders, or liquid preparations, such as oral or sterile parenteral solutions or suspensions.

In order to obtain consistency of administration it is preferred that a composition of the invention is in the form of a unit dose.

Preferably the composition are in unit dosage form. A unit dose will generally contain from 0.1 to 1000 mg of the active compound.

Generally an effective administered amount of a compound of the invention will depend on the relative efficacy of the compound chosen, the severity of the disorder being treated and the weight of the sufferer. However, active compounds will typically be administered once or more times a day for example 2, 3 or 4 times daily, with typical total daily doses in the range of from 0.1 to 800 mg/kg/day.

Suitable dose forms for oral administration may be tablets and capsules and may contain conventional excipients such as binding agents, for example syrup, acacia, gelatin, sorbitol, tragacanth, or polyvinylpyrrolidone; fillers, for example lactose, sugar, maize-starch, calcium phosphate, sorbitol or glycine; tabletting lubricants, for example magnesium stearate; disintegrants, for example starch, polyvinylpyrrolidone, sodium starch glycollate or microcrystalline cellulose; or pharmaceutically acceptable wetting agents such as sodium lauryl sulphate.

The solid oral compositions may be prepared by conventional methods of blending, filling or tabletting. Repeated blending operations may be used to distribute the active agent throughout those compositions employing large quantities of fillers. Such operations are of course conventional in the art. The tablets may be coated according to methods well known in normal pharmaceutical practice, in particular with an enteric coating.

Oral liquid preparations may be in the form of, for example, emulsions, syrups, or elixirs, or may be presented as a dry product for reconstitution with water or other suitable vehicle before use. Such liquid preparations may contain conventional additives such as suspending agents, for example sorbitol, syrup, methyl cellulose, gelatin, hydroxyethylcellulose, carboxymethylcellulose, aluminium stearate gel, hydrogenated edible fats; emulsifying agents, for example lecithin, sorbitan monooleate, or acacia; non-aqueous vehicles (which may include edible oils), for example almond oil, fractionated coconut oil, oily esters such as esters of glycerine, propylene glycol, or ethyl alcohol; preservatives, for example methyl or propyl p-hydroxybenzoate or sorbic acid; and if desired conventional flavouring or colouring agents.

For parenteral administration, fluid unit dosage forms are prepared utilizing the compound and a sterile vehicle, and, depending on the concentration used, can be either suspended or dissolved in the vehicle. In preparing solutions the compound can be dissolved in water for injection and filter sterilized before filling into a suitable vial or

ampoule and sealing. Advantageously, adjuvants such as a local anaesthetic, a preservative and buffering agents can be dissolved in the vehicle. To enhance the stability, the composition can be frozen after filling into the vial and the water removed under vacuum. Parenteral suspensions are prepared in substantially the same manner, except that the compound is suspended in the vehicle instead of being dissolved, and sterilization cannot be accomplished by filtration. The compound can be sterilized by exposure to ethylene oxide before suspending in the sterile vehicle. Advantageously, a surfactant or wetting agent is included in the composition to facilitate uniform distribution of the compound.

The formulations mentioned herein are carried out using standard methods such as those described or referred to in reference texts such as the British and US Pharmacopoeias, Remington's Pharmaceutical Sciences (Mack Publishing Co.), Martindale The Extra Pharmacopoeia (London, The Pharmaceutical Press) or the above mentioned publications.

Suitable methods for preparing and suitable unit dosages for the additional medicament agent, such as the antidiabetic agent mentioned herein include those methods and dosages described or referred to in the above mentioned reference texts.

GSK-3 Assays

Types of GSK-3 assay used to test the compounds of the invention include the following:

Type 1: The GSK-3 specific peptide used in this assay was derived from the phosphorylation site of glycogen synthase and its sequence is: YRRAAVPPSPSLSRHSSPHQ(S)EDEEE. (S) is pre-phosphorylated as is glycogen synthase in vivo and the three consensus sites for GSK-3 specific phosphorylation are underlined. The buffer used to make up the glycogen synthase peptide and [γ-^{33}P] ATP consisted of MOPS 25mM, EDTA 0.2mM, MgAcetate 10mM, Tween-20 0.01% and mercaptoethanol 7.5mM at pH 7.00.

The compounds were dissolved in dimethyl sulphoxide (DMSO) to a final concentration of 100mM. Various concentrations were made up in DMSO and mixed with the substrate (GSK-3 peptide) solution (to a final concentration 20uM) described in the above section along with rabbit or human GSK-3α and GSK-3β (final concentration 0.5U/ml enzyme). The reactions were initiated with the addition of [γ-^{33}P] ATP (500cpm/pmole) spiked into a mixture of ATP (final concentration of 10μM). After 30 min at room temperature the reaction was terminated by the addition of 10μl of H_3PO_4 / 0.01% Tween-20 (2.5%). A volume (10μl) of the mixture was spotted onto P-30 phosphocellulose paper (Wallac & Berthold, EG&G Instruments Ltd, Milton Keynes). The paper was washed four times in H_3PO_4 (0.5%), 2 mins for each wash, air dried and the radioactive phosphate incorporated into the synthetic glycogen synthase peptide, which binds to the P-30 phosphocellulose paper, was counted in a Wallac microbeta scintillation counter.

Analysis of Data: Values for IC_{50} for each inhibitor were calculated by fitting a four-parameter logistic curve to the model : cpm=lower+(upper-lower) /(1 + (concentration/ IC_{50}) ^{slope}).

Type 2: This protocol is based on the ability of the kinase to phosphorylate a biotinylated 26 mer peptide, sequence of which derived from the phosphorylation site of glycogen synthase and its sequence is Biot- YRRAAVPPSPSLSRHSSPHQ(S)EDEEE, with (S) is a pre-phosphorylated serine as is glycogen synthase in vivo and the three consensus sites for GSK-3 specific phosphorylation are underlined. The phosphorylated biotinylated peptide is then captured onto streptavidin coated SPA beads (Amersham Technology), where the signal from the 33P is amplified via the scintillant contained in the beads.

The kinase was assayed at a concentration of 10 nM final in 25 mM MOPS buffer, pH 7.0 containing 0.01% Tween-20, 7.5 mM 2-mercaptoethanol, 10 mM Magnesium acetate, and 10 uM [γ-^{33}P]-ATP. After 60 minutes incubation at room temperature, the reaction was stopped by addition of 50 mM EDTA solution containing the Streptavidin coated SPA beads to give a final 0.5 mgs of beads per assay well in a 384 microtiter plate format.

10 mM stock solutions of the compounds of the invention in 100% DMSO are generated as a first step in the screening process. The second step involves the creation of dose response plates where these compounds are diluted across the plate where the final low and high concentrations are to be 0.008 and 10 uM final in the kinase assay. The third step involves the creation of the assay plates. This is achieved by transferring the compounds from four 96 dose response plates to one 384 assay plate on the Robocon Robolab system. The fourth step is to perform the assay as described and count the resulting plates in the Trilux (Wallac 1450 microbeta liquid scintillation and luminescence counter). The final step is data acquisition and analysis where IC_{50} values are generated for each compound in duplicate by fitting a four parameter logistic curve to the model : cpm = lower + (upper-lower) / (1 + (concentration / IC_{50}) ^{slope}) in a batch manner.

The most potent compounds of the present invention show IC_{50} values in the range of from between 10 to 100 nM.

No adverse toxicological effects are expected for the compounds of the invention, when administered in accordance with the invention.

The following Examples illustrate the invention, but do not limit it in any way.

Example 1

3-(3-Bromophenylamino)-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione

A solution of 3-bromoaniline (2.27 mL, 0.020 mol) and 3-chloro-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione (2.02 g, 0.0083 mol; prepared by analogy with the methods described in WO97/34890 and Wiley, R.H. and Slaymaker, S.C. J. Am. Chem. Soc. (80) 1385 (1958)) in methanol (50 mL) was heated at reflux for 40 hours, cooled and concentrated. The residue was acidified with aqueous hydrochloric acid (1M, 200 mL) and extracted with ethyl acetate (3 x 200 mL). The combined organic solutions were washed with water and brine, dried with magnesium sulphate, evaporated and the residue chromatographed on silica gel using dichloromethane-diethyl ether (gradient from 100:0 to 95:5 v/v) as eluent to afford the title compound as a solid.

^{1}H NMR (DMSO-d_6): δ6.70-7.30 (8H, m), δ9.65 (1H, br), δ10.90 (1H, br).
MS (APCI +ve): $[M+H]^+$ at m/z 377/379/381 ($C_{16}H_{10}BrClN_2O_2$ requires $[M+H]^+$ at m/z 377/379/381).

Example 2

3-(4-Benzoylphenylamino)-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione

A sealed tube (comprising threaded glass tube with resealable cap) containing a mixture of 4-aminobenzophenone (0.147 g, 0.75 mmol), 3-chloro-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione (0.061 g, 0.25 mmol) and 1-methyl-2-pyrrolidinone (0.5 mL) was irradiated in a microwave reactor for 12 minutes at 100 Watts. The mixture was diluted with aqueous hydrochloric acid (5 mL) and extracted with ethyl acetate (2 x 5 mL). The combined organic solutions were evaporated and the residue chromatographed on silica gel using dichloromethane as eluent to afford the title compound as a solid.

^{1}H NMR (DMSO-d_6): δ6.85 (2H, d), δ7.00 (2H, d), δ7.25 (2H, d), δ7.35 (2H, d), δ7.50-7.70 (5H, m), δ9.95 (1H, s), δ10.95 (1H, s)
MS (APCI -ve): $[M]^-$. at m/z 402/404 ($C_{23}H_{15}ClN_2O_3$ requires $[M]^-$. at m/z 402/404)

Example 3

3-(3-Bromo-4-methylphenylamino)-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione

A mixture of 3-bromo-4-methylaniline (0.220 g, 1.18 mmol), 3-chloro-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione (0.100 g, 0.40 mmol) and 1-methyl-2-pyrrolidinone (1.0 mL) was heated in an oil bath at 200°C for 51 minutes. The mixture was diluted with aqueous hydrochloric acid (5 mL) and extracted with ethyl acetate (5 mL). The combined organic solutions were evaporated and the residue chromatographed on silica gel using dichloromethane as eluent to afford the title compound, a solid, following trituration with dichloromethane-hexane (90:10 v/v).

^{1}H NMR ($CDCl_3$): δ2.24 (3H, s), δ6.65-7.70 (7H, m, reduces to 5H on D_2O exchange) and δ8.05 (2H, m).
MS (APCI -ve): $[M-H]^-$ at m/z 400/402 ($C_{17}H_{12}BrN_3O_4$ requires $[M-H]^-$ at m/z 400/402).

Example 4
3-(4-Methylphenylamino)-4-(4-hydroxyphenyl)-1H-pyrrole-2,5-dione
A mixture of 3-hydroxy-4-(4-hydroxyphenyl)-1H-pyrrole-2,5-dione (103 mg, 0.5 mmol) and 4-methylaniline (59 mg, 0.55 mmol) in 1-methyl-2-pyrrolidinone (1mL) was heated in a sealed tube at 150°C for 24hours. The reaction mixture was dissolved in ethyl acetate(20 mL) and washed with 1N HCl (2 x 20 mL), water (3 x 20 mL) and brine (20 mL). The solution was dried over magnesium sulphate, evaporated and the residue chromatographed on silica gel using dichloromethane-diethyl ether (gradient from 100:0 to 90:10 v/v) as eluent to afford the title compound as a solid.

^{1}H NMR (DMSO-d_6): δ2.35 (3H, s), δ6.50 (2H, d), δ6.64 (2H, d), δ6.77 (2H, d), δ6.90 (2H, d), δ9.26 (1H, br), δ9.44 (1H, br), δ10.64 (1H, br).
MS (APCI +ve): $[M+H]^+$ at m/z 295 ($C_{17}H_{14}N_2O_3$ requires $[M+H]^+$ at m/z 295).

Example 5
3-(N-Methyl-N-phenylamino)-4-(indol-3-yl)-1H-pyrrole-2,5-dione.
A mixture of 3-(N-methyl-N-phenylamino)-4-(indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione (Table B, Example B1; 2.00 g, 0.006 mol), aqueous potassium hydroxide solution (10% w/v, 2 L), ethanol (50 mL) and *n*-butanol (200 mL) was heated at reflux for 5 hours. The cooled reaction mixture was filtered and the filtrate acidified to pH 1 by addition of conc. hydrochloric acid. The mixture was cooled to 0°C and the resulting solid filtered, washed with water and recrystallised from acetonitrile to give the corresponding maleic anhydride. This anhydride (0.4 g, 1.25 mmol) was suspended in a mixture of concentrated aqueous ammonium hydroxide and DMF and heated in stainless steel bomb at 130°C for 4 hours. The resulting mixture was diluted with water and extracted with dichloromethane and the dried organic solution evaporated to give a solid. This was chromatographed on silica gel using a gradient of 0-5% (v/v) of methanol in dichloromethane as eluent to afford the title compound, a solid.

^{1}H NMR (DMSO-d_6): δ3.07 (3H, s), δ6.75-7.45 (9H, m), δ7.68 (1H, s), δ10.70 (1H, br) and δ11.70 (1H, br).
MS (APCI +ve): $[M+H]^+$ at m/z 318 ($C_{19}H_{15}N_3O_2$ requires $[M+H]^+$ at m/z 318).

Further elution of the chromatography column afforded 3-amino-4-(indol-3-yl)-1H-pyrrole-2,5-dione (Table B, Example B2) as a byproduct.

Example 6
3-(Indan-5-ylamino)-4-(3-aminophenyl)-1H-pyrrole-2,5-dione

3-(Indan-5-ylamino)-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione (Table A, Example A359; 0.3 g, 0.9 mmol) and 10% Pd/C (60 mg) in ethanol (25 mL) was hydrogenated at atmospheric temperature and pressure for 2 hours. The reaction mixture was filtered through Kieselguhr and the filtrate concentrated in vacuo to give an orange solid. The crude product was taken up in dichloromethane (10 mL) and treated with di-tert-butyl dicarbonate (0.216 g, 1 mmol) and the mixture stirred at ambient temperature for 18 hours. The reaction mixture was poured into saturated aqueous sodium bicarbonate (10 mL) and extracted into dichloromethane (3x10 mL). The combined organics were washed with brine, dried over anhydrous sodium sulfate and concentrated in vacuo. Chromatography on silica gel using dichloromethane-methanol gave the product *amine* as an orange powder.

^{1}H NMR (DMSO-d_6): δ1.85 (2H, quintet), δ2.50 (2H, t), δ2.66 (2H, t), δ4.82 (2H, s), δ5.89 (1H, d), δ6.36 (2H, m), δ6.47 (1H, s), δ6.25 (2H, m), δ6.85 (1H, d), δ9.13 (1H, br) and δ10.58 (1H, br).
MS (APCI +ve): $[M+H]^+$ at m/z 320 ($C_{19}H_{17}N_3O_2$ requires $[M+H]^+$ at m/z 320)

Example 7
3-(Indan-5-ylamino)-4-(3-acetylaminophenyl)-1H-pyrrole-2,5-dione
3-(Indan-5-ylamino)-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione (Table A, Example A359; 0.3 g, 0.9 mmol) and 10% Pd/C (60 mg) in ethanol (25 mL) was hydrogenated at atmospheric temperature and pressure for 2 hours. The reaction mixture was filtered through Kieselguhr and the filtrate concentrated in vacuo to give an orange solid. The crude product was taken up in dichloromethane (5 mL) and treated with acetic anhydride (85 μL, 0.9 mmol) and stirred for 3 hours at ambient temperature. The reaction mixture was poured onto saturated aqueous sodium bicarbonate solution (10 mL) and extracted into ethyl acetate (3x10 mL). The combined organics were washed with brine, dried over anhydrous sodium sulfate and concentrated in vacuo. Chromatography on silica gel using dichloromethane-methanol gave the desired compound as an orange powder.

^{1}H NMR (DMSO-d_6): δ1.83(2H, quintet), δ2.02 (3H, s), δ2.45 (2H, t), δ2.66 (2H, t), δ6.41 (2H, m), δ6.59 (1H, d), δ6.84 (2H, d), δ6.90 (1H, t), δ7.38 (1H, d), δ9.30 (1H, bs), δ9.68 (1H, s) and δ10.61 (1H, bs)]
MS (APCI –ve): $[M-H]^-$ at m/z 360 ($C_{21}H_{19}N_3O_3$ requires $[M-H]^-$ at m/z 360).

Example 8
3-(Indan-5-ylamino)-4-[3-[(3-fluorophenylaminocarbonyl)amino]phenyl]-1H-pyrrole-2,5-dione
3-(Indan-5-ylamino)-4-(3-aminophenyl)-1H-pyrrole-2,5-dione (Table A, Example A599; 0.08 g, 0.3 mmol) in dichloromethane (10 mL) was was treated with 3-fluorophenyl isocyanate (0.038mg, 0.3 mmol). The mixture was shaken on an orbital shaker for 72 hours. Saturated aqueous sodium bicarbonate (5 mL) was added, shaking continued for 5

minutes and the organic layer transferred directly onto a column of silica gel. Elution with dichloromethane gave the product as a yellow solid.

^{1}H NMR (DMSO-d_6): δ1.78 (2H, quintet), δ2.44 (2H, t), δ2.62 (2H, t), δ6.47 (2H, m), δ6.61 (1H, dd), δ6.83 (2H, m), δ6.93 (2H, m), δ7.09 (1H, dd), δ7.28 (2H, m), δ7.45 (1H, dd), δ8.42 (1H, br), δ8.72 (1H, br), δ9.30 (1H, br) and δ10.65 (1H, br).
MS (APCI -ve) $[M]^-$ at m/z 456 ($C_{26}H_{21}FN_4O_3$ requires $[M]^-$ at m/z 456).

Example 9

3-(Indan-5-ylamino)-4-[3-(benzoylamino)phenyl]-1H-pyrrole-2,5-dione

3-(5-Indan-5-ylamino)-4-(3-aminophenyl)-1H-pyrrole-2,5-dione (Table A, Example A599; 0.100 g, 0.3 mmol) in dichloromethane (3 mL) was added to a solution of benzoic acid (0.042 g, 0.33 mmol), 1-hydroxybenzotriazole (0.047 g, 0.33 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.063 g, 0.33 mmol in dichloromethane (5 mL). The mixture was shaken on an orbital shaker for 72 hours. Saturated aqueous sodium bicarbonate (5 mL) was added, shaking continued for 5 minutes and the organic layer transferred directly onto a column of silica gel. Elution with dichloromethane gave the product as a yellow solid.

^{1}H NMR (DMSO-d_6): δ1.83 (2H, quintet), δ2.43 (2H, t), δ2.57 (2H, t), δ6.42 (1H, s), δ6.30 (2H, m), δ6.83 (1H, d), δ7.02 (1H, t), δ7.22 (1H, s), δ7.56 (4H, m), δ7.86 (2H, dd), δ9.38 (1H, br), δ9.98 (1H, br) and δ10.68 (1H, bs).
MS (APCI –ve): $[M-H]^-$ at m/z 422 ($C_{26}H_{21}N_3O_3$ requires $[M-H]^-$ at m/z 422)

Example 10

3-[4-(2-Aminoethyl)phenylamino]-4-(2-methoxyphenyl)-1H-pyrrole-2,5-dione

A solution of 3-[4-[2-(*t*-butoxycarbonylamino)ethyl]phenylamino]-4-(2-methoxyphenyl)-1H-pyrrole-2,5-dione (0.060 g, 0.13 mmol) and trifluoroacetic acid (4 drops) in dry DCM (5 mL) was stirred for 18 hours at room temperature. The suspension was diluted with ethyl acetate (10 mL), poured onto sodium bicarbonate (20 mL) and extracted with ethyl acetate (3 x 10 mL). The combined organic solutions were washed with brine, dried with magnesium sulfate, evaporated and the residue triturated with a mixture of hexane-dichloromethane (95:5 v/v) to afford the title compound as an orange solid.

^{1}H NMR ($CDCl_3$); δ1.52 (2H, br), δ2.59 (2H, t), δ2.83 (2H, t), δ3.16 (3H, s), δ6.44 (1H, d), δ6.58 (2H, d), δ6.79 (2H,d), δ6.97-6.93 (1H, m), δ7.22-7.17 (3H, m) and δ7.33 (1H, d).
MS (APCI +ve): $[M+H]^+$ at m/z 338 ($C_{19}H_{19}N_3O_3$ requires $[M+H]^+$ at 338).

Example 11

3-(3-Fluoro-4-methylphenylamino)-4-[4-(methoxycarbonyl)phenyl]-1H-pyrrole-2,5-dione

A mixture of 3-(3-Fluoro-4-methylphenyl-amino)-4-(4-iodophenyl)-1H-pyrrole-2,5-dione (Example A705, 126 mg, 0.3 mmol), tetrakis(triphenyl phosphine)-palladium(0) (35 mg, 0.03 mmol) and methanol (10 mL) was placed in a 50mL two necked round bottomed flask. One arm of the flask was sealed with a septum and to the other arm was fitted a reflux condenser, topped with a multiway tap connected respectively to vacuum, a carbon monoxide cylinder and to a balloon. Using the multiway tap, the flask was alternately evacuated and flushed with carbon monoxide, and the process repeated several times to unsure an atmosphere of carbon monoxide within the flask. The balloon was charged with carbon monoxide and this was then opened to the reaction flask for the duration of the reaction in order to maintain a slight positive pressure of carbon monoxide within the flask. Triethylamine (100 uL, 0.7 mmol) was added and the mixture heated at reflux for 16 hours. The mixture was cooled and diluted with ethyl acetate and the resulting solution washed with aqueous hydrochloric acid (1M, 50 mL), water (50 mL) and brine (50 mL). The organic solution was dried over magnesium sulphate and evaporated to afford a solid. This was chromatographed on silica gel using dichloromethane-ether (98:2 v/v) as eluent to afford the title compound, a solid.

^{1}H NMR ($CDCl_3$): δ2.14 (3H, s), δ3.90 (3H, s), δ6.35–7.30 (7H, m) and δ7.82 (2H, m).
MS (APCI +ve): $[M+H]^+$ at m/z 355 ($C_{19}H_{15}FN_2O_4$ requires $[M+H]^+$ at 355).

Example 12

3-[4-[2-[N-[6-(Acetylamino)hexyl]aminocarbonyl]ethyl]phenylamino]-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione

A solution of triethylamine (81 mg, 0.8 mmol) in dry N, N-dimethylformamide (5 mL) was added to a mixture of 3-[4-[2-(hydroxycarbonyl)ethyl]phenylamino]-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione (Example A763, 152 mg, 0.4 mmol), N-(6-aminohexyl)acetamide hydrochloride (78 mg, 0.4 mmol), 1-(3-dimethylamino-propyl)-3-ethylcarbodiimide hydrochloride (77 mg, 0.4 mmol) and 1-hydroxybenzotriazole (54 mg, 0.4 mmol) and the resulting mixture stirred at room temperature for 18 hours. The mixture was diluted with ethyl acetate (25 mL) and washed successively with water (2 x 25 mL), saturated aqueous sodium bicarbonate solution (25 mL), water (2 x 25 mL), brine (25 mL), dried over magnesium sulphate and concentrated. The residue was redissolved in dichloromethane-methanol (1:1 v/v), filtered and evaporated to afford the title compound as a foam.

^{1}H NMR (DMSO-d_6); δ1.10-1.40 (8H, m), δ1.77 (3H, s), δ2.15 (2H, m), δ2.55 (2H, m), δ3.00 (4H, m), δ6.62 (2H, d), δ6.77 (2H, d), δ7.20-7.90 (6H, m), δ9.80 (1H, br) and δ10.85 (1H, br).
MS (APCI +ve): $[M+H]^+$ at m/z 522 ($C_{27}H_{31}N_5O_6$ requires $[M+H]^+$ at 522).

Example 13

3-[4-(*trans*-2-carboxyethenyl)phenylamino]-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione

A mixture of *trans*-4-aminocinnamic acid (0.205 g, 1.26 mmol), 3-chloro-4-(4-chlorophenyl)-1H-pyrrole-2.5-dione (0.123 g, 0.51 mmol) and 1-methyl-2-pyrrolidinone (1.0 mL) was heated in a sealed tube in a hotblock set at 69°C for 28.5 hours. The mixture was diluted with aqueous hydrochloric acid (10 mL) and extracted with ethyl acetate (2x20 mL). The combined organics were washed with brine (2x10 mL), dried over anhydrous magnesium sulphate and evaporated to dryness. The residue was triturated with a mixture of dichloromethane and ethyl acetate to afford the title compound as a solid.

^{1}H NMR (DMSO-d_6): δ6.35 (1H, d), 6.74 (2H, d), 6.99 (2H, d), 7.19(2H, d), 7.35 (2H, d), 7.42 (1H, d), 9.76 (1H, br), 10.89(1H, br) and δ12.23 (1H, br).
MS (APCI +ve): $[M+H]^+$ at m/z 369/371 ($C_{19}H_{13}N_2O_4$ requires $[M+H]^+$ at m/z 369/371).

Example 14
3-[4-(*trans*-2-carbamoylethenyl)phenylamino]-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione

3-[4-[*trans*-2-(ethoxycarbonyl)ethenyl]phenylamino)-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione (50mg, 0.126mmol) was dissolved in 2N methanolic ammonia (5ml) and allowed to stand at room temp for 12days. Aqueous ammonia (d 0.88, 5ml) was added and the solution stood at room temp for a further 8 days. The mixture was evaporated to dryness and the residue triturated with methanol then ether to give the title compound as a solid.

1H NMR (DMSO-d_6): δ10.75(1H, br), δ9.7 (1H, br), δ7.44 (1H, br), δ7.2 (5H, m), δ7.2 (3H, m), δ6.74 (2H, d), δ6.41 (1H, d).
MS (APCI +ve): $[M+H]^+$ at m/z 368/370 ($C_{19}H_{14}ClN_3O_3$ requires $[M+H]^+$ at m/z 368/370).

Example 15
3-(Indol-1-yl)-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione

Sodium hydride (60% dispersion in mineral oil, 30 mg, 0.75 mmol) was added to a solution of indole (88 mg, 0.75 mmol) in THF (2 mL) at room temperature. The mixture was stirred for 30 minutes prior to the addition of a solution of 1-(*tert*-butyldimethylsilyl)-3-chloro-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione (Procedure method 1, 180 mg, 0.5 mmol) in THF (1 mL). The mixture was stirred for 45 minutes then diluted with ethyl acetate (80 mL), washed with dilute hydrochloric acid (20 mL), dried ($MgSO_4$) and concentrated. The residue was chromatographed on silica gel using a gradient of hexane-ethyl acetate to afford the title compound, a solid.

^{1}H NMR (CD_3OD); δ6.42 (1H, d), 6.77 (1H, d), 6.82 (1H, t), 7.00-7.60 (5H, m) and 8.05-8.25 (2H, m).
MS (APCI +ve): $[M+H]^+$ at m/z 334 ($C_{18}H_{11}N_3O_4$ requires $[M+H]^+$ at 334).

Example 16

3-Amino-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione

3-chloro-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione (1.0 g, 4 mmol) was suspended in a mixture of ethanol (20 mL) and aqueous 880 ammonia (5 mL) and the mixture heated to 80°C whilst ammonia gas was bubbled through the mixture for 4 hours. The mixture was cooled and concentrated and the residue chromatographed on silica gel using hexane-ethyl acetate (gradient from 1:1 v/v) as eluent to afford the title compound as a solid.

^{1}H NMR (CD_3COCD_3); δ6.77 (2H, br), 7.60 (1H, t), 8.04 (2H, m), 8.50 (1H, t) and 9.33 (1H, br).

MS (APCI +ve): $[M+H]^+$ at m/z 234 ($C_{10}H_7N_3O_4$ requires $[M+H]^+$ at 234).

Example 17

3-[4-[2-methoxyethylaminocarbonylmethylthio]phenylamino]-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione

A solution of 2-methoxyethylamine in THF (0.32M, 1 mL) was added to a mixture of 3-[4-(carboxymethylthio)phenylamino]-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione (Example A941, 117 mg, 0.3 mmol), 1-(3-dimethylamino-propyl)-3-ethylcarbodiimide hydrochloride (57 mg, 0.3 mmol) and 1-hydroxybenzotriazole (40 mg, 0.3 mmol) in dry THF (1 mL). The resulting solution was stirred at room temperature for 57 hours, then diluted with ethyl acetate (50 mL) and washed with dilute hydrochloric acid (1M, 50 ml), water (50 mL) and brine (50 mL), dried over magnesium sulphate and evaporated. The resulting gum was chromatographed on silica gel using dichloromethane-methanol (98:2 v/v) as eluent to afford the title compound, a solid.

^{1}H NMR (DMSO-d_6) d 3.20 (3H, s), 3.21 (2H, m), 3.25 (2H, t), 3.50 (2H, s), 6.60-7.20 (8H, m), 8.10 (1H, t, exchanges with D_2O), 9.65 (1H, br, exchanges with D_2O) and 10.82 (1H, br, exchanges with D_2O).

MS (APCI+ve) $[M+H]^+$ at m/z 446/448. $C_{21}H_{20}ClN_3O_4S$ requires $[M+H]^+$ at m/z 446/448.

Example 18

3-(2-Methoxyethylamino)-4-(4-iodophenyl)-1H-pyrrole-2,5-dione

A solution of 3-(3-fluoro-4-methylphenylamino)-4-(4-iodophenyl)-1H-pyrrole-2,5-dione (Example A705, 126 mg, 0.3 mmol) and 2-methoxyethylamine (0.2 mL, 2.3 mmol) in DMF (2 mL) was stirred at room temperature for 113 hours then diluted with hydrochloric acid (0.5M, 50 mL) and extracted with ethyl acetate (50 mL). The ethyl acetate solution was washed with water (2 x 50 mL) and brine (50 mL), dried over magnesium sulphate and evaporated. The residue was chromatographed on silica gel using dichloromethane-diethyl ether (99:1 v/v) as eluent to afford the title compound, a solid.

^{1}H NMR ($CDCl_3$): 3.25 (2H, m), 3.35 (3H, s), 3.40 (2H, t), 5.67 (1H, br, exchanges with D_2O), 6.95 (1H, br, exchanges with D_2O), 7.05 (2H, d) and 7.70 (2H, d).
MS (APCI+ve) $[M+H]^+$ at m/z 373. $C_{13}H_{13}IN_2O_3$ requires $[M+H]^+$ at m/z 373.

Example 19
3-Amino-1-[4-(4-chlorophenyl)-2,5-dioxo-1H-pyrrol-3-yl]pyridinium chloride
A mixture of 3-chloro-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione (100 mg, 0.41 mmol) and 3-aminopyridine (42.7 mg, 0.45 mmol) in dry THF (2.5 mL) was heated at 50°C for 2 hours then stirred at room temperature overnight. The resulting suspension was filtered and the solid washed with dichloromethane (20 mL), then hexane (10 mL) to give the title compound as a solid.

^{1}H NMR (DMSO): δ7.07 (2H,br), δ7.43 (2H,d), δ7.61 (2H,d), δ7.93-7.81 (2H,m), δ8.10-8.07 (2H,m) and δ12.07 (1H,br).
MS (APCI+ve): $[M+H]^+$ at m/z 301/303 ($C_{15}H_{11}N_3O_2Cl$ requires $[M+H]^+$ at m/z 301/303)

Example 20
3-[5-methoxy-6-[4-ethylpiperazin-1-yl]-indolin-1-yl]-4-[3-fluorophenyl]-1H-pyrrole-2,5-dione

A solution of 3-chloro-4-(3-fluorophenyl)-1H-pyrrole-2,5-dione (100 mg, 0.44 mmol.), 5-methoxy-6-[4-ethylpiperazin-1-yl]-indoline (156 mg, 0.44 mmol.) and triethylamine (0.12 mL, 0.88 mmol.) in dry 1-methylpyrrolidin-2-one (2 mL) was heated under argon at 65 C for 36 h. The mixture was allowed to stand overnight at RT then diluted with water (80 mL) and extracted with ethyl acetate (3 x 60 mL). The combined organic solutions were washed with water (2 x 60 mL), brine, dried with magnesium sulphate, evaporated and the residue triturated with a mixture of dichloromethane and hexane to afford the title compound as a solid.

^{1}H NMR (DMSO-d_6): δ10.80 (1H, br), δ 7.23-7.17 (1H, m), δ 7.00 (1H, t), δ 6.92-6.85 (3H, m), δ 5.44 (1H, s), δ 4.42 (2H, t), δ 3.71 (3H, s), δ 3.12 (2H, t), δ 2.29 (10H, br.s), δ 0.96 (3H, t)
MS (APCI+ve) : $[M+H]^+$ at m/z 451 ($C_{25}H_{27}N_4O_3F$ requires $[M+H]^+$ at m/z 451)

Example 21
3-[2-(Hydroxymethyl)indolin-1-yl]-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione single enantiomer
A solution of racemic 3-[2-(Hydroxymethyl)indolin-1-yl]-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione (Example D102, 30mg) in acetone (1ml) was separated into it's two enantiomers by repeated high pressure liquid chromatography of aliquots of the solution. The chromatography was performed on a waters 6000 instrument equipped with a 10mm chiracel AD column using hexane-ethanol (85:15 v/v) as eluent at 5 ml min^{-1}. The solvent

was removed at reduced pressure to give the separated enantiomers as solids. Enantiomer 1 (12mg, 100% chiral purity), enantiomer 2 (11mg, 96% chiral purity).

^{1}H NMR (MeOH): δ 2.07-2.25 (2H,m), 2.48 (1H,dd), 2.65 (1H,dd), 4.10 (1H,hept), 4.45 (1H,d), 5.33 (1H,t), 5.52 (1H,t), 5.95 (1H, d), 6.16 (1H,t), 6.42 (1H, d), 6.78 (1H,dd), 6.85 (1H, d).
MS (APCI+ve) $[M+H]^+$ at m/z 366. ($C_{19}H_{15}IN_3O_5$ requires $[M+H]^+$ at m/z 366).

Example 22

3-(3,5-Di-fluorophenylamino)-4-(2,3-di-fluorophenyl)-1H-pyrrole-2,5-dione

A solution of 3,5-difluoroaniline (161 mg, 0.00125 mol) and 3-chloro-4-(2,3-di-fluorophenyl)-1H-pyrrole-2,5-dione (122 mg, 0.0005mol) in methanol (2 mL) was heated in a sealed tube at 65°C for 8 days. The mixture was acidified with aqueous hydrochloric acid (1M) and extracted with ethyl acetate. The combined organic solutions were washed with water and brine, dried with magnesium sulphate, evaporated and the residue triturated with hexane-dichloromethane (95:5 v/v) to afford the title compound as a solid.

^{1}H NMR (DMSO-d_6): δ6.40 (2H, m), δ6.75 (1H, m), δ7.00-7.40 (3H, m), δ10.00 (1H, br) and δ11.00 (1H, br).
MS (APCI +ve): $[M+H]^+$ at m/z 337 ($C_{16}H_8F_4N_2O_2$ requires $[M+H]^+$ at m/z 337).

Procedure Method 1

1-(*tert*-Butyldimethylsilyl)-3-chloro-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione

Triethylamine (1.1 mL, 8 mmol) was added to a stirred suspension of *tert*-butylchlorodimethylsilane (0.66 g, 4.4 mmol) and 3-chloro-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione (1.0 g, 4 mmol) in dichloromethane (15 mL) at room temperature. The mixture was stirred overnight then chromatographed directly on silica gel using a hexane-acetone gradient to afford the title compound.

^{1}H NMR ($CDCl_3$); δ0.51 (6H, s), 0.98 (9H, s), 7.70 (1H, t), 8.27 (2H, m) and 8.80 (1H, m).
MS (APCI –ve): $[M-H]^-$ at m/z 366/368 ($C_{16}H_{19}ClN_2O_4Si$ requires $[M-H]^-$ at 366/368).

The following additional procedures (Procedure Methods 2 & 3) serve to illustrate a typical preparation of a non commercial aniline, by a method analogous to that described in *Synthesis* 1994, 1413.:-

Procedure Method 2

3-[(4-Nitrophenyl)thio]benzoic acid

A suspension of potassium carbonate (18g) in acetone (140 mL) at ambient temperature was treated with 3-mercaptobenzoic acid (10g, 64.4 mmol, 1 eq) followed by 4-nitrofluorobenzene (18g, 127.7 mmol, 2 eq). The resultant mixture was stirred for 18h

and then poured onto saturated sodium bicarbonate and washed with ethyl acetate. The basic aqueous layer was acidified with 5N HCl and extracted into ethyl acetate (3x100 mL). The combined organics were dried with anhydrous sodium sulphate and concentrated *in vacuo* to give the product as a solid.

^{1}H NMR (DMSO): δ7.35 (2H, d), 7.66 (1H, t), 7.81 (1H, m), 8.06 (2H, m), 8.16 (2H, d), and 13.31 (1H, bs).
MS (APCI-ve): $[M-H]^-$ at m/z 274 ($C_{13}H_9NO_4S$ requires $[M-H]^-$ at m/z 274)

Procedure Method 3

3-[(4-Aminophenyl)thio]benzoic acid

A mixture of 3-[(4-nitrophenyl)thio]benzoic acid (11.2g, 40.7 mmol) and 10% Pd/C (0.5g) in ethanol (250 mL) was hydrogenated at atmospheric temperature and pressure for 24h. The mixture was filtered through Celite and concentrated *in vacuo* to give the required aniline as a solid.

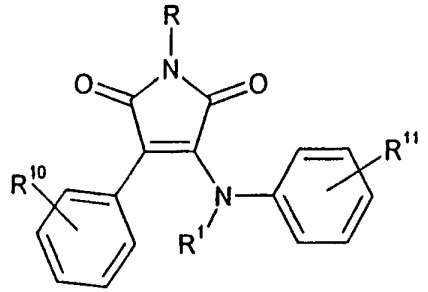
^{1}H NMR (DMSO): δ5.59 (2H, bs), 6.64 (2H, d), 7.28 (3H, m), 7.37 (1H, t), 7.52 (1H, s), 7.65 (1H, d), and 12.32 (1H, bs).MS (APCI+ve): $[M+H]^+$ at m/z 246 ($C_{13}H_{11}NO_2S$ requires $[M+H]^+$ at m/z 246).

The further examples described herein were prepared according to the methods disclosed herein, with particular reference to Examples 1 to 22 above. Examples 1 to 22 themselves are shown as examples A1, A2, A3, A424, B3, A599, F1, F2, F6, A702, A770, A772, A832, A833, D19, B25, A968, B28, I3, D36, D109 and A929 respectively in Tables A, B, D, F and I.

The following tables of examples illustrate the invention, but do not limit it in any way.

Table A

Encompassing compounds of general formula (XXX-1), wherein group R^2 of formula (I) is a phenyl ring, optionally substituted by one or more substituents R^{10} and group R^3 of formula (I) is a phenyl ring, optionally substituted by one or more substituents R^{11} and substituents R, R^1, R^{10} and R^{11} are listed in Table A.



(XXX-1)

Example No.	R	R^1	R^{10}	R^{11}	$[M+H]^+$ Observed; (Unless $[M]^-$ or $[M-H]^-$ are Indicated)	For Procedure See Example No.
A1	H	H	4-Cl	3-Br	377/379/381	1
A2	H	H	4-Cl	4-COPh	402/404 [M]-	2

A3	H	H	3-NO2	3-Br-4-Me	400/402 [M-H]-	3
A4	H	H	H	H	265	1
A5	Me	H	H	H	279	1
A6	H	H	H	4-OMe	295	1
A7	H	H	H	4-Me	279	1
A8	H	H	H	4-Cl	299/301	1
A9	H	H	H	2-Me	277 [M-H]-	1
A10	H	H	H	2-OMe	295	1
A11	H	H	H	4-O*n*Bu	337	1
A12	H	H	H	4-*n*Bu	321	1
A13	Me	H	H	4-Cl	313/315	1
A14	Me	H	H	4-OMe	309	1
A15	Et	H	H	H	293	1
A16	Et	H	H	4-Cl	327/329	1
A17	Et	H	H	4-OMe	323	1
A18	Ph	H	H	H	341	1
A19	Ph	H	H	4-Cl	375/377	1
A20	Ph	H	H	4-OMe	371	1
A21	CH2Ph	H	H	H	355	1
A22	CH2Ph	H	H	4-Cl	389	1
A23	CH2Ph	H	H	4-OMe	385	1
A24	H	H	H	4-SMe	311	1
A25	H	H	H	4-(1-Morpholinyl)	350	1
A26	H	H	H	3-SMe	311	1
A27	H	H	H	3-OPh	357	1
A28	H	H	H	4-F	283	1

A29	H	H	4-Cl	4-OMe	329/331	1
A30	H	H	4-OMe	2-OMe	325	1
A31	H	H	4-OMe	4-O*n*Bu	367	1
A32	H	H	4-OMe	3-OPh	387	1
A33	H	H	4-OMe	3-SMe	341	1
A34	H	H	4-OMe	4-F	313	1
A35	H	H	4-OMe	4-SMe	341	1
A36	H	H	4-OMe	4-*n*Bu	351	1
A37	H	H	4-OMe	H	295	1
A38	H	H	4-OMe	4-Cl	329/331	1
A39	H	H	4-Cl	3-Cl	333/335/337	1
A40	H	H	4-Cl	2-OMe	329/331	1
A41	H	H	4-Cl	4-O*n*Bu	371/373	1
A42	H	H	4-Cl	3-OPh	391/393	1
A43	H	H	4-Cl	3-SMe	345/347	1
A44	H	H	4-Cl	4-CF3	367/369	1
A45	H	H	4-Cl	4-F	317/319	1
A46	H	H	4-Cl	4-SMe	345/347	1
A47	H	H	4-Cl	3-CF3	367/369	1
A48	H	H	4-Cl	4-*n*Bu	355/357	1
A49	H	H	4-Cl	H	299/301	1
A50	H	H	4-Cl	2-Me-4-Cl	347/349/351	1
A51	H	H	4-Cl	4-Cl	333/335/337	1
A52	H	H	4-Cl	2-Me	313/315	1
A53	H	H	4-Cl	2,3-[(-CH=CH-)2]	349/351	1
A54	H	H	2,3-[(-CH=CH-)2]	4-O*n*Bu	387	1

A55	H	H	2,3-[(-CH=CH-)2]	4-F	331 [M-H]-	1
A56	H	H	2,3-[(-CH=CH-)2]	4-SMe	361	1
A57	H	H	2,3-[(-CH=CH-)2]	4-*n*Bu	371	1
A58	H	H	2,3-[(-CH=CH-)2]	H	315	1
A59	H	H	4-OMe	4-OMe	325	1
A60	H	H	4-OMe	3-Cl	329/331	1
A61	H	H	4-OMe	2-Me	309	1
A62	H	H	3,4,5-tri-OMe	4-OMe	385	1
A63	H	H	3,4,5-tri-OMe	H	355	1
A64	H	H	H	3-Cl	299	1
A65	H	H	4-CF3	2-Me	345 [M-H]-	1
A66	H	H	4-CF3	2-Et	359 [M-H]-	1
A67	H	H	4-CF3	2-*i*Pr	375	1
A68	H	H	4-CF3	2-F	349 [M-H]-	1
A69	H	H	4-CF3	2-Cl	365/367 [M-H]-	1
A70	H	H	4-CF3	2-SMe	379	1
A71	H	H	4-CF3	3-SMe	379	1
A72	H	H	4-CF3	3-Me	345 [M-H]-	1
A73	H	H	4-CF3	3-Et	361	1
A74	H	H	4-CF3	3-OMe	363	1
A75	H	H	4-CF3	3-Cl	365/367	1
A76	H	H	4-CF3	3-F	349 [M-H]-	1
A77	H	H	4-CF3	3-Br	409/411 [M-H]-	1
A78	H	H	4-CF3	3-I	457 [M-H]-	1
A79	H	H	4-CF3	3-OCH2Ph	439	1
A80	H	H	4-CF3	3-CONH2	375 [M]-	1

A81	H	H	3,4,5-tri-OMe	4-Cl	389/391	1
A82	H	H	4-Cl	2-Et	327/329	1
A83	H	H	4-Cl	2-*i*Pr	341/343	1
A84	H	H	4-Cl	2-F	317/319	1
A85	H	H	4-Cl	2-SMe	345/347	1
A86	H	H	4-Cl	3-Me	313/315	1
A87	H	H	4-Cl	3-Et	327/329	1
A88	H	H	4-Cl	3-OMe	329/331	1
A89	H	H	4-Cl	3-F	315/317 [M-H]-	1
A90	H	H	4-Cl	3-I	423/425 [M-H]-	1
A91	H	H	4-Cl	3-OCH2Ph	405/407	1
A92	H	H	4-Cl	3-CONH2	342/344	1
A93	H	H	2-CF3	3-SMe	377 [M-H]-	1
A94	H	H	2-CF3	3-Me	347	1
A95	H	H	2-CF3	3-Et	361	1
A96	H	H	4-OMe	4-Me	309	1
A97	H	H	4-OMe	4-*t*Bu	351	1
A98	H	H	4-OMe	3,4-[(CH2)3]	335	1
A99	H	H	4-OMe	3,5-di-Me	323	1
A100	H	H	4-OMe	3-OCH2Ph	401	1
A101	H	H	4-OMe	3-OMe	325	1
A102	H	H	4-OMe	3-I	421	1
A103	H	H	4-OMe	3,4-[OCH2O]	339	1
A104	H	H	4-OMe	3,5-di-OMe	355	1
A105	H	H	3-OMe	4-*n*Bu	351	1
A106	H	H	3-OMe	3-OPh	387	1

A107	H	H	3-OMe	4-SMe	341	1
A108	H	H	3-OMe	4-Me	309	1
A109	H	H	3-OMe	4-*t*Bu	351	1
A110	H	H	3-OMe	3,5-di-Me	323	1
A111	H	H	3-OMe	3-OCH2Ph	401	1
A112	H	H	3-OMe	3-OMe	325	1
A113	H	H	3-OMe	3-I	421	1
A114	H	H	3-OMe	3,4-[OCH2O]	339	1
A115	H	H	3-OMe	3,5-di-OMe	355	1
A116	H	H	3-OMe	4-OMe	325	1
A117	H	H	3-OMe	3,4-[(CH2)3]	335	1
A118	H	H	3-OMe	4-SCF3	395	1
A119	H	H	2-OMe	4-*n*Bu	351	1
A120	H	H	2-OMe	3-OPh	387	1
A121	H	H	2-OMe	4-SMe	341	1
A122	H	H	2-OMe	4-Me	309	1
A123	H	H	2-OMe	4-*t*Bu	351	1
A124	H	H	2-OMe	3,4-[(CH2)3]	335	1
A125	H	H	2-OMe	3,5-di-Me	323	1
A126	H	H	2-OMe	3-OCH2Ph	401	1
A127	H	H	2-OMe	3-OMe	325	1
A128	H	H	2-OMe	3-I	421	1
A129	H	H	2-OMe	3,5-di-OMe	355	1
A130	H	H	2-OMe	4-OMe	325	1
A131	H	H	2-OMe	3-CF3	363	1
A132	H	H	4-OMe	3-CF3	363	1

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A133	H	H	3-OMe	3-CF3	363	1
A134	H	H	2-OMe	3,4-[OCH2O]	339	1
A135	H	Me	4-CF3	H	347	1
A136	H	H	4-CF3	H	333	2
A137	H	H	4-CF3	2,3-[(-CH=CH-)2]	383	2
A138	H	H	4-CF3	4-CF3	401	2
A139	H	H	4-CF3	4-CN	358	2
A140	H	H	4-CF3	4-COPh	437	2
A141	H	H	2-CF3	H	333	2
A142	H	H	2-CF3	2-Me	347	2
A143	H	H	4-CF3	2-Me-4-Cl	381/383	2
A144	H	H	4-OMe	3-CH2OH	325	1
A145	H	H	H	2,3-[(-CH=CH-)2]	315	1
A146	H	H	4-Cl	3-OH	315/317	1
A147	H	Me	H	H	279	1
A148	H	Me	4-Ph	H	355	1
A149	H	Me	4-Cl	H	313/315	1
A150	H	Me	4-OMe	H	309	1
A151	H	Me	3-NO2	H	324	1
A152	H	Me	3-OMe	H	309	1
A153	H	H	4-CF3	4-CO2H	377	2
A154	H	H	4-Ph	4-Me	355	1
A155	H	H	4-Ph	4-O*n*Bu	412 [M]-	1
A156	H	H	4-Ph	4-*n*Bu	397	1
A157	H	H	4-Ph	4-SMe	387	1
A158	H	H	4-Ph	2-Me	355	1

A159	H	H	4-Ph	3-SMe	387	1
A160	H	H	4-Ph	3-OPh	433	1
A161	H	H	4-Ph	3-Cl	375/377	1
A162	H	H	4-Ph	3-COMe	383	1
A163	H	H	4-Ph	3-Br	417/419 [M-H]-	1
A164	H	H	4-Ph	3-(5-Oxazolyl)	407 [M]-	1
A165	H	H	4-Ph	3-OH	357	1
A166	H	H	3-NO2	4-Me	324	1
A167	H	H	3-NO2	4-O*n*Bu	382	1
A168	H	H	3-NO2	4-SMe	356	1
A169	H	H	3-NO2	2-Me	324	1
A170	H	H	3-NO2	3-SMe	356	1
A171	H	H	3-NO2	3-OPh	402	1
A172	H	H	3-NO2	3-Cl	344/346	1
A173	H	H	3-NO2	3,5-di-Cl	376/378/380 [M-H]-	1
A174	H	H	3-NO2	3-COMe	350 [M-H]-	1
A175	H	H	3-NO2	3-Br	388/390	1
A176	H	H	3-NO2	3-(5-Oxazolyl)	375 [M-H]-	1
A177	H	H	3-NO2	3-OH	326	1
A178	H	H	3-NO2	4-*n*Bu	366	1
A179	H	H	4-CF3	4-NO2	378	2
A180	H	H	3,4,5-tri-OMe	4-Me	369	1
A181	H	H	3,4,5-tri-OMe	4-O*n*Bu	427	1
A182	H	H	3,4,5-tri-OMe	4-*n*Bu	411	1
A183	H	H	3,4,5-tri-OMe	4-SMe	401	1
A184	H	H	3,4,5-tri-OMe	3-SMe	401	1

A185	H	H	3,4,5-tri-OMe	3-COMe	397	1
A186	H	H	3,4,5-tri-OMe	3-(5-Oxazolyl)	422	1
A187	H	H	3,4,5-tri-OMe	3-OH	371	1
A188	H	H	H	4-CF3	333	1
A189	H	H	4-OMe	4-(CH2)2OH	337 [M-H]-	1
A190	H	H	H	4-(CH2)2OH	309	1
A191	H	H	2-Cl	4-OMe	329	1
A192	H	H	H	3-CF3	331 [M-H]-	1
A193	H	H	4-Cl	4-CN	323/325 [M]-	2
A194	H	H	4-CF3	2,4,6-tri-Me	375	2
A195	H	H	4-Cl	2,3-[(CH2)4]	353/355	1
A196	H	H	4-Cl	4-*t*Bu	355/357	1
A197	H	H	4-Cl	4-CH2P(O)(OEt)2	449/451	1
A198	H	H	4-Cl	4-OPh	391/393	1
A199	H	H	4-Cl	4-(Cyclohexyl)	381/383	1
A200	H	H	4-Cl	2-CH2Ph	389/391	1
A201	H	H	4-Cl	4-Br-3-Cl	411/413/415/417	1
A202	H	H	4-Cl	4-I-3-Cl	459/461/463	1
A203	H	H	4-Cl	3,4-di-Cl	367/369/371/373	1
A204	H	H	4-Cl	3,5-di-Cl	367/369/371/373	1
A205	H	H	4-Cl	3,5-di-Cl-4-OH	383/385/387/389	1
A206	H	H	4-Cl	3,5-di-F	335/337	1
A207	H	H	4-Cl	4-Br	377/379/381	1
A208	H	H	4-Cl	4-I	425/427	1
A209	H	H	4-Cl	3-NO2	344/346	1
A210	H	H	4-Cl	2-OH	315/317	1

A211	H	H	4-Cl	4-OH	315/317	1
A212	H	H	4-Cl	3,5-di-Br-4-Me	469/471/473/475	1
A213	H	H	4-Cl	3,4-[OCH2O]	343/345	1
A214	H	H	4-Cl	3,4-[CH=N-NH]	339/341	1
A215	H	H	4-Cl	3,4-[NH-N=CH]	339/341	1
A216	H	H	4-Cl	3-Br-2-Me	391/393/395	1
A217	H	H	4-Cl	3-Br-4-Me	391/393/395	1
A218	H	H	4-Cl	3-Cl-2-Me	347/349/351	1
A219	H	H	4-Cl	3-F-4-Me	331/333	1
A220	H	H	4-Cl	3-F-6-Me	331/333	1
A221	H	H	4-Cl	4-Me	313/315	1
A222	H	H	4-Cl	2-CH2OH	329/331	1
A223	H	H	4-Cl	3-CH2OH	329/331	1
A224	H	H	4-Cl	4-OH-2-Me	329/331	1
A225	H	H	4-Cl	4-NHCOMe	356/358	1
A226	H	H	4-Cl	2,3-di-Me	327/329	1
A227	H	H	4-Cl	2,4-di-Me	327/329	1
A228	H	H	4-Cl	3,4-di-Me	327/329	1
A229	H	H	4-Cl	3,5-di-Me	327/329	1
A230	H	H	4-Cl	3-CH2OH-6-Me	343/345	1
A231	H	H	4-Cl	4-OMe-2-Me	343/345	1
A232	H	H	4-Cl	4-(CH2)2OH	343/345	1
A233	H	H	4-Cl	3,5-di-OMe	359/361	1
A234	H	H	4-Cl	4-CH2CN	338/340	1
A235	H	H	4-Cl	3,4-[CH=CH-NH]	338/340	1
A236	H	H	4-Cl	3-COMe	341/343	1

A237	H	H	4-Cl	4-CH2CO2H	357/359	1
A238	H	H	4-Cl	3,4-[(CH2)3]	337/339 [M-H]-	1
A239	H	H	4-Cl	4-N(Me)COMe	370/372	1
A240	H	H	4-Cl	3-O*i*Pr	357/359	1
A241	H	H	4-Cl	4-(CH2)2CONH2	370/372	1
A242	H	H	3,4-[OCH2O]	3-OPh	401	1
A243	H	H	4-Cl	4-CONH2	340/342 [M-H]-	3
A244	H	H	4-F	2-Me	297	1
A245	H	H	4-F	3-SMe	329	1
A246	H	H	4-F	3-Cl	317/319	1
A247	H	H	4-F	4-Cl-2-Me	331/333	1
A248	H	H	4-F	3-OPh	375	1
A249	H	H	4-F	4-SMe	329	1
A250	H	H	4-F	4-*t*Bu	339	1
A251	H	H	4-F	3,4-[(CH2)3]	323	1
A252	H	H	2-OMe	3-Me	309	1
A253	H	H	2-OMe	3-F	313	1
A254	H	H	2-OMe	2-F	313	1
A255	H	H	2-OMe	4-Cl-2-Me	343/345	1
A256	H	H	2-OMe	2-Me	309	1
A257	H	H	2-OMe	3-SMe	341	1
A258	H	H	3-Cl	2-Me	313/315	1
A259	H	H	3-Cl	3-SMe	345/347	1
A260	H	H	3-Cl	3-Cl	333/335/337	1
A261	H	H	3-Cl	4-Cl-2-Me	347/349/351	1
A262	H	H	3-Cl	3-OPh	391/393	1

A263	H	H	3-Cl	4-SMe	345/347	1
A264	H	H	3-Cl	4-*t*Bu	355/357	1
A265	H	H	3-Cl	3,4-[(CH2)3]	339/341	1
A266	H	H	3,4-[(-CH=CH-)2]	3-Me	329	1
A267	H	H	3,4-[(-CH=CH-)2]	3-F	333	1
A268	H	H	3,4-[(-CH=CH-)2]	4-Cl-2-Me	363/365	1
A269	H	H	3,4-[(-CH=CH-)2]	2-Me	329	1
A270	H	H	3,4-[(-CH=CH-)2]	3-SMe	361	1
A271	H	H	3,4-[(-CH=CH-)2]	3-Cl	349/351	1
A272	H	H	4-I	2-Me	405	1
A273	H	H	4-I	3-SMe	437	1
A274	H	H	4-I	3-Cl	425/427	1
A275	H	H	4-I	4-Cl-2-Me	439/441	1
A276	H	H	4-I	3-OPh	483	1
A277	H	H	4-I	4-SMe	437	1
A278	H	H	4-I	4-*t*Bu	447	1
A279	H	H	4-I	3,4-[(CH2)3]	431	1
A280	H	H	4-OMe	3-Me	309	1
A281	H	H	4-OMe	3-F	313	1
A282	H	H	3-OMe	2-Me	309	1
A283	H	H	3-OMe	3-SMe	341	1
A284	H	H	3-OMe	3-Cl	329/331	1
A285	H	H	2-OMe	3-Cl	329/331	1
A286	H	H	4-F	3-Br	361/363	1
A287	H	H	4-OMe	3-Br	373/375	1
A288	H	H	3,4-[(-CH=CH-)2]	3-Br	393/395	1

A289	H	H	4-I	3-Br	469/471	1
A290	H	H	4-Cl	4-NO2	342/344 [M-H]-	3
A291	H	H	3,4-di-Cl	3-Br	411/413/415/417	1
A292	H	H	3-Cl	3-Br	377/379/381	1
A293	H	H	2-Cl	3-OPh	391/393	3
A294	H	H	2-Cl	3-Cl	333/335	3
A295	H	H	2-Cl	3-SMe	345/347	1
A296	H	H	2-Cl	4-SMe	345/347	1
A297	H	H	3-OMe	4-CONH2	337 [M]-	3
A298	H	H	4-Cl	4-CO2H	297/299 Fragment ion [M-CO2H]-	3
A299	H	H	4-OMe	4-CN	320	3
A300	H	H	2-Cl	4-*n*Bu	355/357	1
A301	H	H	2-Cl	3-Br	375/377/379 [M]-	1
A302	H	H	2-Cl	4-Me	313/315	1
A303	H	H	4-Cl	3-Cl-6-Me	347/349/351	3
A304	H	H	3-NO2	3-Cl-4-Me	356/358 [M-H]-	3
A305	H	H	3-NO2	4-COPh	414	3
A306	H	H	3,5-di-F	3-Br	379/381	1
A307	H	H	3-CF3	3-Br	411/413	1
A308	H	H	4-Me	3-Br	357/359	1
A309	H	H	4-Br	3-SMe	389/391	1
A310	H	H	4-Br	4-Me	357/359	1
A311	H	H	4-Br	3,5-di-Cl	409/411/413/415 [M-H]-	1
A312	H	H	4-Br	3-OPh	435/437	1

A313	H	H	4-Br	3,4-[(CH2)3]	383/385	1
A314	H	H	4-Me	3-SMe	325	1
A315	H	H	4-Me	4-Me	293	1
A316	H	H	4-Me	3-OPh	371	1
A317	H	H	4-Me	3,4-[(CH2)3]	319	1
A318	H	H	4-Me	4-SMe	325	1
A319	H	H	4-SMe	3-SMe	357	1
A320	H	H	4-SMe	4-Me	325	1
A321	H	H	4-SMe	3-OPh	403	1
A322	H	H	4-SMe	3,4-[(CH2)3]	351	1
A323	H	H	4-SMe	4-SMe	357	1
A324	H	H	3-CF3	3-SMe	379	1
A325	H	H	3-CF3	4-Me	347	1
A326	H	H	3-CF3	3,5-di-Cl	399/401/403 [M-H]-	1
A327	H	H	3-CF3	3-OPh	425	1
A328	H	H	3-CF3	3,4-[(CH2)3]	373	1
A329	H	H	3-CF3	4-SMe	379	1
A330	H	H	3,5-di-F	3-SMe	347	1
A331	H	H	3,5-di-F	4-Me	315	1
A332	H	H	3,5-di-F	3,5-di-Cl	367/369/371 [M]-	1
A333	H	H	3,5-di-F	3-OPh	393	1
A334	H	H	3,5-di-F	3,4-[(CH2)3]	341	1
A335	H	H	3,5-di-F	4-SMe	347	1
A336	H	H	3,4-di-Cl	3-SMe	379/381/383	1
A337	H	H	3,4-di-Cl	4-Me	347/349/351	1
A338	H	H	3,4-di-Cl	3,5-di-Cl	399/401/403/405/407	1

					[M-H]-	
A339	H	H	3,4-di-Cl	3-OPh	423/425/427 [M]-	1
A340	H	H	3,4-di-Cl	3,4-[(CH2)3]	373/375/377	1
A341	H	H	3,4-di-Cl	4-SMe	379/381/383	1
A342	H	H	3-Br	3-SMe	389/391	1
A343	H	H	3-Br	4-Me	355/357 [M]-	1
A344	H	H	3-Br	3,5-di-Cl	409/411/413/415 [M-H]-	1
A345	H	H	3-Br	3-OPh	435/437	1
A346	H	H	3-Br	3,4-[(CH2)3]	383/385	1
A347	H	H	3-Br	4-SMe	389/391	1
A348	H	H	4-NO2	3-SMe	356	1
A349	H	H	4-NO2	4-Me	324	1
A350	H	H	4-NO2	3,5-di-Cl	376/378/380 [M-H]-	1
A351	H	H	4-NO2	3-OPh	402	1
A352	H	H	4-NO2	3,4-[(CH2)3]	350	1
A353	H	H	4-NO2	4-SMe	356	1
A354	H	H	4-Br	4-SMe	389/391	1
A355	H	H	3-NO2	4-NO2	353 [M]-	3
A356	H	H	3-NO2	3,5-di-Cl-4-OH	392/394/396 [M-H]-	1
A357	H	H	3-NO2	4-*t*Bu	366	1
A358	H	H	3-NO2	3,5-di-Br-4-OH	482/484/486	1
A359	H	H	3-NO2	3,4-[(CH2)3]	350	1
A360	H	H	3-NO2	3-Br-4-OCF3	470/472[M-H]-	1
A361	H	H	3-NO2	3-Br-5-CF3	454/456[M-H]-	1
A362	H	H	3-NO2	4-CH2CN	349	1

A363	H	H	3-NO2	4-(CH2)2CONH2	381	1
A364	H	H	3-NO2	3-F	326[M-H]-	1
A365	H	H	3-NO2	3-F-4-Me	342	1
A366	H	H	3-NO2	4-Cl	342/344[M-H]-	1
A367	H	H	3-NO2	4-OMe	340	1
A368	H	H	3-NO2	3-Et	338	1
A369	H	H	3-NO2	2-F	328	1
A370	H	H	3-NO2	3,5-di-F	344[M-H]-	1
A371	H	H	3-NO2	3,4-[S-CH=N]	367	1
A372	H	H	3-NO2	4-OPh	402	1
A373	H	H	3-NO2	4-*trans*-CH=CHCO2H	378[M-H]-	1
A374	H	H	3-NO2	4-OCH2Ph	416	1
A375	H	H	3-NO2	3-CO(CH2)2CO2Me	422[M-H]-	1
A376	H	H	3-NO2	3-NO2	353 [M]-	3
A377	H	H	3-NO2	4-CN	333 [M]-	3
A378	H	H	4-Cl	4-OH-3-CO2H	359/361	1
A379	H	H	4-Cl	3-CO2H	341/343 [M-H]-	1
A380	H	H	4-Cl	4-SCH2CO2Me	403/405	1
A381	H	H	4-Cl	4-OH-3-NO2	360/362	1
A382	H	H	4-Cl	4-(CH2)2CO2H	371/373	1
A383	H	H	4-Cl	4-Cl-3-CO2H	375/377/379 [M-H]-	1
A384	H	H	4-Cl	4-(CH2)3CO2H	385/387	1
A385	H	H	4-Cl	3-SO2CF3	429/431[M-H]-	1
A386	H	H	4-Cl	3-COPh	403/405	1
A387	H	H	4-Cl	3,5-di-Br-4-OH	471/473/475/477	1
A388	H	H	4-Cl	4-CPh3	541/543	1

A389	H	H	4-Cl	3-CH2CO2H	355/357 [M-H]-	1
A390	H	H	4-Cl	4-(1-Adamantyl)	433/435	1
A391	H	H	4-Cl	3-CO2H-4-[S-(2-CO2H-Ph)]	373/375 Fragment ion [M-C7H5O2]-	1
A392	H	H	4-Cl	2-[O(CH2)2OMe]-5-(CH2)2CO2H	443/445 [M-H]-	1
A393	H	H	4-Cl	3-Br-4-Cl	411/413/415/417	1
A394	H	H	4-Cl	2-OPh	391/393	1
A395	H	H	4-Cl	4-CH2SO2NHMe	311/313 Fragment ion [M – CH4NO2S]+	1
A396	H	H	3-NO2	4-CO2H	352 [M-H]-	3
A397	H	H	3-NO2	3-COPh	414	3
A398	H	H	4-Cl	3-CH2CO2Me	371/373	1
A399	H	H	4-OH	3-Br	359/361	4
A400	H	H	4-Br	4-COPh	447/449	3
A401	H	H	4-SMe	4-COPh	415	3
A402	H	H	4-OH	4-SMe	327	4
A403	H	H	4-*i*Pr	3-SMe	351[M-H]-	1
A404	H	H	4-*i*Pr	4-Me	319[M-H]-	1
A405	H	H	4-*i*Pr	3,4-[(CH2)3]	345[M-H]-	1
A406	H	H	3,5-di-Me	3-SMe	337[M-H]-	1
A407	H	H	3,5-di-Me	4-Me	305[M-H]-	1
A408	H	H	3,5-di-Me	3,4-[(CH2)3]	331[M-H]-	1
A409	H	H	3,5-di-Me	4-SMe	337[M-H]-	1
A410	H	H	4-*i*Pr	4-SMe	351[M-H]-	1

A437	H	H	4-OH	3-Br-4-Me	371/373[M-H]-	4
A438	H	H	4-OH	3,4-[(CH2)3]	321	4
A439	H	H	3,5-di-Me	3-OPh	383[M-H]-	1
A440	H	H	2-Br	3-OPh	434[M-H]-	1
A441	H	H	3,5-bis-CF3	3-OPh	492[M]-	1
A442	H	H	4-OCH2Ph	3-OPh	461[M-H]-	1
A443	H	H	3-Cl-4-OMe	3-OPh	419/421 [M-H]-	1
A444	H	H	3,4-di-OMe	3-OPh	415[M-H]-	1
A445	H	H	4-OPh	3-OPh	447[M-H]-	1
A446	H	H	4-OCH2Ph	4-Me	383[M-H]-	1
A447	H	H	2-Cl	3-Cl-4-Me	347/349/351	3
A448	H	H	3,4-[OCH2O]	3-SMe	353[M-H]-	1
A449	H	H	3,4-[OCH2O]	4-Me	323	1
A450	H	H	3,4-[OCH2O]	3,4-[(CH2)3]	349	1
A451	H	H	3,4-[OCH2O]	4-SMe	355	1
A452	H	H	3,4-[OCH2O]	3-Br	387/389	1
A453	H	H	3,4-[OCH2O]	3-Br-4-Me	401/403	1
A454	H	H	2-Me	4-Me	293	1
A455	H	H	2-Me	3,4-[(CH2)3]	319	1
A456	H	H	2-Me	4-SMe	325	1
A457	H	H	3-Me	3-OPh	371	1
A458	H	H	3-Br	4-Cl	375/377/379 [M-H]-	1
A459	H	H	4-*i*Pr	3-OPh	397[M-H]-	1
A460	H	H	4-CH2OMe	3-SMe	353[M-H]-	1
A461	H	H	4-CH2OMe	4-Me	321[M-H]-	1
A462	H	H	4-CH2OMe	H	307[M-H]-	1

A411	H	H	2-Br	3-SMe	387/389[M-H]-	1
A412	H	H	2-Br	4-Me	355/357[M-H]-	1
A413	H	H	2-Br	3,4-[(CH2)3]	381/383[M-H]-	1
A414	H	H	2-Br	4-SMe	387/389[M-H]-	1
A415	H	H	3,5-bis-CF3	3-SMe	446[M]-	1
A416	H	H	3,5-bis-CF3	4-Me	414[M]-	1
A417	H	H	3,5-bis-CF3	3,5-di-Cl	468/470/472 [M]-	1
A418	H	H	3,5-bis-CF3	3,4-[(CH2)3]	440[M]-	1
A419	H	H	3,5-bis-CF3	4-SMe	446[M]-	1
A420	H	H	4-OPh	3-SMe	401[M-H]-	1
A421	H	H	4-OPh	4-Me	369[M]-	1
A422	H	H	4-OPh	3,4-[(CH2)3]	395[M-H]-	1
A423	H	H	4-OPh	4-SMe	401[M-H]-	1
A424	H	H	4-OH	4-Me	295	4
A425	H	H	4-OCH2Ph	3-SMe	415[M-H]-	1
A426	H	H	4-OCH2Ph	3,4-[(CH2)3]	409[M-H]-	1
A427	H	H	4-OCH2Ph	4-SMe	415[M-H]-	1
A428	H	H	3,4-di-OMe	3-SMe	371	1
A429	H	H	3,4-di-OMe	4-Me	337[M-H]-	1
A430	H	H	3,4-di-OMe	3,4-[(CH2)3]	363[M-H]-	1
A431	H	H	3-Cl-4-OMe	4-SMe	373/375 [M-H]-	1
A432	H	H	3-Cl-4-OMe	3-SMe	373/375 [M-H]-	1
A433	H	H	3-Cl-4-OMe	4-Me	341/343 [M-H]-	1
A434	H	H	3-Cl-4-OMe	3,4-[(CH2)3]	369/371	1
A435	H	H	3-NO2	4-COMe	352	3
A436	H	H	4-OH	3-OPh	371[M-H]-	4

A463	H	H	4-CH2OMe	3-OPh	399[M-H]-	1
A464	H	H	4-CH2OMe	3,4-[(CH2)3]	347[M-H]-	1
A465	H	H	4-CH2OMe	4-SMe	353[M-H]-	1
A466	H	H	4-CH2OMe	3-Br	385/387[M-H]-	1
A467	H	H	4-CH2OMe	3-Br-4-Me	399/401[M-H]-	1
A468	H	H	2-Me	4-Cl	313/315	1
A469	H	H	2,5-di-OMe	3-SMe	369[M-H]-	1
A470	H	H	2,5-di-OMe	4-Me	337[M-H]-	1
A471	H	H	2,5-di-OMe	H	323[M-H]-	1
A472	H	H	2,5-di-OMe	3-OPh	415[M-H]-	1
A473	H	H	2,5-di-OMe	3,4-[(CH2)3]	363[M-H]-	1
A474	H	H	2,5-di-OMe	4-SMe	369[M-H]-	1
A475	H	H	2,5-di-OMe	3-Br	401/403 [M-H]-	1
A476	H	H	2,5-di-OMe	3-Br-4-Me	415/417[M-H]-	1
A477	H	H	4-OCF3	3-SMe	393[M-H]-	1
A478	H	H	4-OCF3	4-Me	361[M-H]-	1
A479	H	H	4-OCF3	H	347[M-H]-	1
A480	H	H	4-OCF3	3-OPh	439[M-H]-	1
A481	H	H	4-OCF3	3,4-[(CH2)3]	387[M-H]-	1
A482	H	H	4-OCF3	3-Br	425/427[M-H]-	1
A483	H	H	4-OCF3	3-Br-4-Me	439/441 [M-H]-	1
A484	H	H	4-OCF3	4-SMe	393[M-H]-	1
A485	H	H	3-SCF3	3-SMe	409[M-H]-	1
A486	H	H	3-SCF3	4-Me	377[M-H]-	1
A487	H	H	3-SCF3	H	363[M-H]-	1
A488	H	H	3-SCF3	3-OPh	455[M-H]-	1

A489	H	H	3-SCF3	3,4-[(CH2)3]	403[M-H]-	1
A490	H	H	3-SCF3	4-SMe	409[M-H]-	1
A491	H	H	3-SCF3	3-Br	441/443[M-H]-	1
A492	H	H	3-SCF3	3-Br-4-Me	455/457[M-H]-	1
A493	H	H	3-Cl	4-Cl	333/335/337	1
A494	H	H	4-Cl	3,4-[S-CH=N]	356/358	1
A495	H	H	2-OMe	3,4-[S-CH=N]	352	1
A496	H	H	4-OMe	3,4-[S-CH=N]	352	1
A497	H	H	4-Br	4-CH=CHCO2H	411/413 [M-H]-	1
A498	H	H	4-Br	4-CH(OMe)Me	401/403	1
A499	H	H	2-Me	3-SMe	325	1
A500	H	H	2-Me	3-Br-4-Me	371/373	1
A501	H	H	3-F	3-SMe	329	1
A502	H	H	3-F	4-Me	297	1
A503	H	H	3-F	3,5-di-Cl	351/353/355	1
A504	H	H	3-F	3-OPh	375	1
A505	H	H	3-F	3,4-[(CH2)3]	323	1
A506	H	H	3-F	4-SMe	329	1
A507	H	H	3-F	3-Br	361/363	1
A508	H	H	3-F	3-Br-4-Me	375/377	1
A509	H	H	2,4-di-Cl	3-SMe	379/381/383	1
A510	H	H	2,4-di-Cl	4-Me	347/349/350	1
A511	H	H	2,4-di-Cl	3-OPh	425/427/429	1
A512	H	H	2,4-di-Cl	3,4-[(CH2)3]	373/375/377	1
A513	H	H	2,4-di-Cl	4-SMe	379/381/383	1
A514	H	H	2,4-di-Cl	3-Br	411/413/415/417	1

A515	H	H	2,4-di-Cl	3-Br-4-Me	425/427/429/431	1
A516	H	H	3-Me	3-SMe	325	1
A517	H	H	3-Me	4-Me	293	1
A518	H	H	3-Me	3,4-[(CH2)3]	319	1
A519	H	H	3-Me	4-SMe	325	1
A520	H	H	3-Me	3-Br	357/359	1
A521	H	H	3-Me	3-Br-4-Me	371/373	1
A522	H	H	4-Cl-3-NO2	3-SMe	388/390[M-H]-	1
A523	H	H	4-Cl-3-NO2	4-Me	356/358[M-H]-	1
A524	H	H	4-Cl-3-NO2	3,5-di-Cl	410/412/414/416[M-H]-	1
A525	H	H	4-Cl-3-NO2	3-OPh	434/436[M-H]-	1
A526	H	H	4-Cl-3-NO2	3,4-[(CH2)3]	384/386	1
A527	H	H	4-Cl-3-NO2	4-SMe	390/392	1
A528	H	H	4-Cl-3-NO2	3-Br-4-Me	434/436/438[M-H]-	1
A529	H	H	4-OH	3,4-[S-CH=N]	338	4
A530	H	H	4-SMe	3,4-[S-CH=N]	368	1
A531	H	H	4-I	3,4-[S-CH=N]	448	1
A532	H	H	2-Cl	3,4-[S-CH=N]	356/358	1
A533	H	H	4-Cl-3-NO2	3-Br	420/422/424[M-H]-	1
A534	H	H	3-NO2	3-CH2OH	338[M-H]-	1
A535	H	H	3-NO2	3-CONH2	351[M-H]-	1
A536	H	H	3-NO2	3-OCH2CO2Et	410[M-H]-	1
A537	H	H	3-NO2	3,4-di-Me	336[M-H]-	1
A538	H	H	3-NO2	3-CO2H	352[M-H]-	1
A539	H	H	3-NO2	3,4-[OCH2O]	352[M-H]-	1

A540	H	H	3-NO2	3-CH2CO2Me	380[M-H]-	1
A541	H	H	3-NO2	3-OCH2CO2Me	396[M-H]-	1
A542	H	H	4-Br	3-Cl-4-Me	391/393/395	1
A543	H	H	4-Me	3-Cl-4-Me	327/329	1
A544	H	H	4-SMe	3-Cl-4-Me	359/361	1
A545	H	H	2-OMe	3-Cl-4-Me	343/345	1
A546	H	H	4-OMe	3-Cl-4-Me	343/345	1
A547	H	H	2-Cl	3-Br-4-Me	391/393/395	1
A548	H	H	4-Br	3-Br-4-Me	435/437/439	1
A549	H	H	4-Me	3-Br-4-Me	371/373	1
A550	H	H	4-SMe	3-Br-4-Me	403/405	1
A551	H	H	2-OMe	3-Br-4-Me	387/389	1
A552	H	H	4-OMe	3-Br-4-Me	387/389	1
A553	H	H	2-Cl	H	299/301	1
A554	H	H	4-Br	H	343/345	1
A555	H	H	4-Me	H	279	1
A556	H	H	4-SMe	H	311	1
A557	H	H	2-OMe	H	295	1
A558	H	H	3-NO2	3-Cl-4-OH	358/360 [M-H]-	1
A559	H	H	3-NO2	3-Cl-4-OMe	374/376	1
A560	H	H	3-NO2	3-F-4-OMe	358	1
A561	H	H	3-NO2	3,5-di-Br	464/466/468 [M-H]-	1
A562	H	H	3-NO2	3,5-di-Br-4-Me	478/480/482 [M-H]-	1
A563	H	H	3-NO2	3,5-di-Me	338	1
A564	H	H	3-NO2	H	310	1
A565	H	H	2-Me	3-OPh	371	1

A566	H	H	3-NO2	4-(CH2)2OH	352 [M-H]-	1
A567	H	H	3-NO2	4-CH2CO2H	366 [M-H]-	1
A568	H	H	3-NO2	4-CH2P(O)(OEt)2	460	1
A569	H	H	3-NO2	4-CH2SO2NHMe	415 [M-H]-	1
A570	H	H	3-NO2	4-SCH2CO2H	398 [M-H]-	1
A571	H	H	3-NO2	4-OH	324 [M-H]-	1
A572	H	H	3-NO2	4-(CH2)3CO2H	394 [M-H]-	1
A573	H	H	3-NO2	4-CH2CO2Me	380 [M-H]-	1
A574	H	H	3-NO2	4-SCH2CO2Me	412 [M-H]-	1
A575	H	H	3-NO2	4-(CH2)3CO2Me	410	1
A576	H	H	3-NO2	3,4-[CH=N-NH]	350	1
A577	H	H	3-NO2	3,4-[NH-N=CH]	350	1
A578	H	H	4-Me	3,4-[S-CH=N]	336	1
A579	H	H	4-Br	3,4-[S-CH=N]	400/402	1
A580	H	H	3,5-di-F	3,4-[S-CH=N]	358	1
A581	H	H	3-NO2	2-Ph	384 [M-H]-	1
A582	H	H	2-OMe	3-Et	323	1
A583	H	H	2-OMe	3-OH	311	1
A584	H	H	2-OMe	3-Br	373/375	1
A585	H	H	2-OMe	3-COMe	337	1
A586	H	H	2-OMe	3-COPh	399	1
A587	H	H	2-OMe	3-F-4-Me	327	1
A588	H	H	2-OMe	3,5-di-Br-4-OH	467/469/471	1
A589	H	H	2-OMe	4-CH2CN	334	1
A590	H	H	2-OMe	4-(CH2)2CONH2	366	1
A591	H	H	2-OMe	4-Cl	329/321	1

A592	H	H	2-OMe	4-OPh	387	1
A593	H	H	2-OMe	4-OCH2Ph	401	1
A594	H	H	2-OMe	3-F-4-OMe	343	1
A595	H	H	2-OMe	3-Cl-4-OMe	357/359 [M-H]-	1
A596	H	H	2-OMe	3-Cl-4-OH	345/347	1
A597	H	H	2-OMe	4-Br-3-Cl	407/409/411	1
A598	H	H	2-OMe	3-Br-4-OCF3	457/459	1
A599	H	H	3-NH2	3,4-[(CH2)3]	320	6
A600	H	H	4-SMe	2-Ph	385 [M-H]-	1
A601	H	H	3-NO2	4-I	435 [M]-	1
A602	H	H	2-OMe	3-NO2	340	1
A603	H	H	2-OMe	3,5-di-F	331	1
A604	H	H	2-OMe	3-Br-5-CF3	441/443	1
A605	H	H	2-OMe	3,5-di-Cl-4-OH	379/381/383	1
A606	H	H	2-OMe	4-*trans*-CH=CHCO2H	363 [M-H]-	1
A607	H	H	3-OPh	4-Me	371	1
A608	H	H	3-OPh	3-Br	433/435 [M-H]-	1
A609	H	H	3-OPh	4-SMe	401 [M-H]-	1
A610	H	H	3-OPh	3-OPh	447 [M-H]-	1
A611	H	H	3-OPh	3,4-[(CH2)3]	395 [M-H]-	1
A612	H	H	3-OPh	H	357	1
A613	H	H	3-OPh	3-SMe	403	1
A614	H	H	3-OPh	3-Br-4-Me	447/449 [M-H]-	1
A615	H	H	4-O*n*Bu	4-Me	349 [M-H]-	1
A616	H	H	4-O*n*Bu	3-OPh	428 [M]-	1
A617	H	H	4-O*n*Bu	3,4-[(CH2)3]	377	1

A618	H	H	4-O*n*Bu	H	337	1
A619	H	H	4-O*n*Bu	3-SMe	383	1
A620	H	H	4-O*n*Bu	3-Br-4-Me	427/429 [M-H]-	1
A621	H	H	2,6-di-Cl	4-Me	347/349/351	1
A622	H	H	2,6-di-Cl	H	331/333/335 [M-H]-	1
A623	H	H	2,6-di-Cl	3-SMe	377/379/381 [M-H]-	1
A624	H	H	4-SMe	3-Br	389/391	1
A625	H	H	4-SMe	3-Cl	345/347	1
A626	H	H	3,5-di-F	3-NO2	344 [M-H]-	1
A627	H	H	2-Cl	3,4-di-Me	327/329	1
A628	H	H	4-Br	3,4-di-Me	369/371 [M-H]-	1
A629	H	H	4-Br	3-Br	419/421/423 [M-H]-	1
A630	H	H	4-Br	3-Cl	375/377/379 [M-H]-	1
A631	H	H	3-Br	3-NO2	386/388 [M-H]-	1
A632	H	H	2-OMe	3,4-di-Me	323	1
A633	H	H	3-OMe	3,4-di-Me	323	1
A634	H	H	3-OPh	3,4-di-Me	385	1
A635	H	H	4-SMe	3,4-di-Me	337 [M-H]-	1
A636	H	H	3-OPh	4-Br	433/435 [M-H]-	1
A637	H	H	4-Me	3-Cl	313/315	1
A638	H	H	2-OMe	4-(CH2)2NHCO2*t*Bu	436 [M-H]-	1
A639	H	H	3-NO2	2,3-[(CH2)4]	362 [M-H]-	1
A640	H	H	3-Cl	3-NO2	342/344 [M-H]-	1
A641	H	H	2-OMe	4-CH2NHCO2*t*Bu	422 [M-H]-	1
A642	H	H	4-O*n*Bu	4-SMe	383	1
A643	H	H	4-C(OMe)2Ph	3-Cl	417/419 Fragment	1

					ion [M-OMe]+	
A644	H	H	4-COPh	3-Cl	403/405	1
A645	H	H	3-NO2-4-OMe	3-Cl	374/376	1
A646	H	H	2-NO2	3-Cl	344/346	1
A647	H	H	2,4-di-OMe	3-SMe	369[M-H]-	1
A648	H	H	2,4-di-OMe	4-Me	337[M-H]-	1
A649	H	H	2,4-di-OMe	H	323[M-H]-	1
A650	H	H	2,4-di-OMe	3-OPh	415[M-H]-	1
A651	H	H	2,4-di-OMe	3,4-[(CH2)3]	363[M-H]-	1
A652	H	H	2,4-di-OMe	4-SMe	369[M-H]-	1
A653	H	H	2,4-di-OMe	3-Br	403/404	1
A654	H	H	2,4-di-OMe	3-Br-4-Me	415/417[M-H]-	1
A655	H	H	3-NO2	3-Cl-4-SMe	388/390 [M-H]-	1
A656	H	H	2-OMe	3-Cl-4-SMe	373/375 [M-H]-	1
A657	H	H	3-NO2	4-CH2NHBoc	437 [M-H]-	1
A658	H	H	4-Br	4-NMe2	386/388	1
A659	H	H	2-OMe	4-NMe2	338	1
A660	H	H	3-NO2	4-NMe2	353	1
A661	H	H	3-NO2	3-OMe	373/375	1
A662	H	H	3-NO2	3-OMe	340	1
A663	H	H	4-Br	3,4-di-OMe	403/405	1
A664	H	H	2-OMe	3,4-di-OMe	355	1
A665	H	H	3-NO2	3,4-di-OMe	370	1
A666	H	H	4-SO2Me	3-Br-4-Me	433/435[M-H]-	1
A667	H	H	4-SO2Me	3-Br	419/421[M-H]-	1
A668	H	H	4-SO2Me	4-SMe	388[M]-	1

A669	H	H	4-SO2Me	3,4-[(CH2)3]	382[M]-	1
A670	H	H	4-SO2Me	3-OPh	434[M]-	1
A671	H	H	4-SO2Me	H	342[M]-	1
A672	H	H	4-SO2Me	4-Me	356[M]-	1
A673	H	H	4-SO2Me	3-SMe	388[M]-	1
A674	H	H	2-F	3-SMe	327[M-H]-	1
A675	H	H	2-F	4-Me	295[M-H]-	1
A676	H	H	2-F	3-OPh	373[M-H]-	1
A677	H	H	2-F	3,4-[(CH2)3]	321[M-H]-	1
A678	H	H	2-F	4-SMe	327[M-H]-	1
A679	H	H	2-F	3-Br	359/361[M-H]-	1
A680	H	H	2-F	3-Br-4-Me	373/375[M-H]-	1
A681	H	H	2,3-di-F	3-Br-4-Me	391/393[M-H]-	1
A682	H	H	2,3-di-F	3-Br	377/379[M-H]-	1
A683	H	H	2,3-di-F	4-SMe	345[M-H]-	1
A684	H	H	2,3-di-F	3,4-[(CH2)3]	339[M-H]-	1
A685	H	H	2,3-di-F	3-OPh	391[M-H]-	1
A686	H	H	2,3-di-F	H	299[M-H]-	1
A687	H	H	2,3-di-F	4-Me	313[M-H]-	1
A688	H	H	2,3-di-F	3-SMe	345[M-H]-	1
A689	H	H	3-NO2	3,4-[N=N-NH]	351	1
A690	H	Me	3-NO2	2-Me	338	1
A691	H	H	3-NO2	2-OH	326	1
A692	H	H	3-NO2	3-CF3	376[M-H]-	1
A693	H	H	3-NO2	3-OCH2Ph	414[M-H]-	1
A694	H	H	3-NO2	3-CO2H-4-Cl	386[M-H]-	1

A695	H	H	3-NO2	3-CO2Me	368	1
A696	H	H	3-NO2	2-OMe	340	1
A697	H	H	3-NO2	3-I	436	1
A698	H	H	3-NO2	3-CO2Me-4-Cl	402/404	1
A699	H	H	3-NO2-4-OMe	3,4-[(CH2)3]	380	1
A700	H	H	3-NO2-4-OMe	3-Br-4-Me	432/434	1
A701	H	H	3-NO2	4-(CH2)2NHBoc	451 [M-H]-	1
A702	H	H	2-OMe	4-(CH2)2NH2	338	10
A703	H	H	2-F	H	281[M-H]-	1
A704	H	H	4-Br	4-CH2NHBoc	470/472 [M-H]-	
A705	H	H	4-I	3-F-4-Me	421 [M-H]-	1
A706	H	H	2-OCH2Ph	3-Cl	405/407	1
A707	H	H	2-Cl	3,5-di-Cl-4-OH	383/385/387/389	1
A708	H	H	2-Cl	3,5-di-Br-4-OH	471/473/475/477	1
A709	H	H	2-Cl	3-CO2H-4-Cl	377/379/381	1
A710	H	H	2-Cl	3-CO2H	343/345	1
A711	H	H	2-Cl	3-OH	315/317	1
A712	H	H	2-Cl	3,4-[OCH2O]	343/345	1
A713	H	H	2-Cl	3,4-[(CH2)3]	339/341	1
A714	H	H	H	3,5-di-Cl-4-OH	349/351/353	1
A715	H	H	H	3,5-di-Br-4-OH	437/439/441	1
A716	H	H	H	3-CO2H-4-Cl	343/345	1
A717	H	H	H	3-CO2H	309	1
A718	H	H	H	3-OH	281	1
A719	H	H	H	3,4-[OCH2O]	309	1
A720	H	H	H	3,4-[(CH2)3]	305	1

A721	H	H	3-NO2-4-OMe	H	340	1
A722	H	H	3-NO2-4-OMe	4-SMe	386	1
A723	H	H	4-Br	3,5-di-Cl-4-OH	427/429/431/433	1
A724	H	H	4-Br	3,5-di-Br-4-OH	515/517/519/521	1
A725	H	H	4-Br	3-CO2H-4-Cl	419/421/423 [M-H]-	1
A726	H	H	4-Br	3-CO2H	387/389	1
A727	H	H	4-Br	3-OH	359/361	1
A728	H	H	4-Br	3,4-[OCH2O]	387/389	1
A729	H	H	4-I	3,5-di-Cl-4-OH	475/477/479	1
A730	H	H	4-I	3,5-di-Br-4-OH	563/565/567	1
A731	H	H	4-I	3-CO2H-4-Cl	469/471	1
A732	H	H	4-I	3-CO2H	435	1
A733	H	H	4-I	3-OH	407	1
A734	H	H	4-I	3,4-[OCH2O]	435	1
A735	H	H	3-Me	3,5-di-Cl-4-OH	363/365/367	1
A736	H	H	3-Me	3,5-di-Br-4-OH	451/453/455	1
A737	H	H	3-Me	3-CO2H-4-Cl	357/359	1
A738	H	H	3-Me	3-CO2H	323	1
A739	H	H	3-Me	3-OH	295	1
A740	H	H	3-Me	3,4-[OCH2O]	323	1
A741	H	H	3-F	3,5-di-Cl-4-OH	367/369/371	1
A742	H	H	3-F	3,5-di-Br-4-OH	455/457/459	1
A743	H	H	3-F	3-CO2H-4-Cl	361/363	1
A744	H	H	3-F	3-CO2H	327	1
A745	H	H	3-F	3-OH	299	1
A746	H	H	3-F	3,4-[OCH2O]	327	1

A747	H	H	4-OMe	3,5-di-Cl-4-OH	379/381/383	1
A748	H	H	4-OMe	3,5-di-Br-4-OH	467/469/471	1
A749	H	H	4-OMe	3-CO2H	339	1
A750	H	H	4-OMe	3-OH	311	1
A751	H	H	3-OMe	3,5-di-Cl-4-OH	379/381/383	1
A752	H	H	3-OMe	3,5-di-Br-4-OH	467/469/471	1
A753	H	H	3-OMe	3-CO2H-4-Cl	373/375	1
A754	H	H	3-OMe	3-CO2H	339	1
A755	H	H	3-OMe	3-OH	311	1
A756	H	H	3-NO2	4-CH2NH2	337 [M-H]-	10
A757	H	H	2-OMe	4-CH2NH2	322 [M-H]-	10
A758	H	H	3-Me	3,4-[S-CH=N]	336	1
A759	H	H	3-OMe	3,4-[S-CH=N]	352	1
A760	H	H	4-OH	3-CO2H-4-Cl	359/361	4
A761	H	H	4-NMe2	4-SMe	354	1
A762	H	H	4-Cl	3-OH-4-OMe	345/347	1
A763	H	H	3-NO2	4-(CH2)2CO2H	380[M-H]	1
A764	H	H	3-NO2	4-(CH2)2CO2Me	396	1
A765	H	H	4-Cl	4-(CH2)2CO2Me	385/387	1
A766	H	H	2-OMe	4-(CH2)2CO2H	367	1
A767	H	H	2-OMe	4-(CH2)2CO2Me	381	1
A768	H	H	4-Cl	3,5-di-Cl-4-Me	381/383/385/387	1
A769	H	H	4-Cl	4-*trans*-CH=CHCO2Et	397/399	1
A770	H	H	4-CO2Me	3-F-4-Me	355	11
A771	H	Me	4-Cl	2-Me	327/329	1

A772	H	H	3-NO2	4-[(CH2)2CONH(CH2)6-NHCOMe]	522	12
A773	H	H	4-Cl	4-[(CH2)2CONH(CH2)6-NHCOMe]	511/513	12
A774	H	H	2-OMe	4-[(CH2)2CONH(CH2)6-NHCOMe]	507	12
A775	H	H	3,5-di-Me	3,5-di-Cl-4-OH	377/379/381	1
A776	H	H	3,5-di-Me	3,5-di-Br-4-OH	465/467/469	1
A777	H	H	3,5-di-Me	3-CO2H-4-Cl	371/373	1
A778	H	H	3,5-di-Me	3-CO2H	337	1
A779	H	H	3,5-di-Me	3-OMe	323	1
A780	H	H	3,5-di-Me	3,4-[OCH2O]	337	1
A781	H	H	4-*i*Pr	3,5-di-Cl-4-OH	391/393/395	1
A782	H	H	4-*i*Pr	3,5-di-Br-4-OH	479/481/483	1
A783	H	H	4-*i*Pr	3-CO2H-4-Cl	385/387	1
A784	H	H	4-*i*Pr	3-CO2H	351	1
A785	H	H	4-*i*Pr	3-OMe	337	1
A786	H	H	4-*i*Pr	3,4-[OCH2O]	351	1
A787	H	H	2-Br	3,5-di-Cl-4-OH	427/429/431/433	1
A788	H	H	2-Br	3,5-di-Br-4-OH	515/517/519/521	1

A789	H	H	2-Br	3-CO2H	387/389	1
A790	H	H	2-Br	3-OMe	373/375	1
A791	H	H	2-Br	3,4-[OCH2O]	387/389	1
A792	H	H	3,4-di-OMe	3-OMe	355	1
A793	H	H	3-Cl-4-OMe	3,5-di-Cl-4-OH	413/415/417/419	1
A794	H	H	3-Cl-4-OMe	3,5-di-Br-4-OH	501/503/505/507	1
A795	H	H	3-Cl-4-OMe	3-CO2H-4-Cl	407/409/411	1
A796	H	H	3-Cl-4-OMe	3-CO2H	371/373 [M-H]-	1
A797	H	H	3-Cl-4-OMe	3-OMe	359/361	1
A798	H	H	4-Me	3,5-di-Cl-4-OH	363/365/367	1
A799	H	H	4-Me	3,5-di-Br-4-OH	451/453/455	1
A800	H	H	4-Me	3-CO2H	323	1
A801	H	H	4-Me	3-OMe	309	1
A802	H	H	4-Me	3,4-[OCH2O]	323	1
A803	H	H	2,4-di-Cl	3,5-di-Cl-4-OH	415/417/419/421/423 [M-H]-	1
A804	H	H	2,4-di-Cl	3,5-di-Br-4-OH	503/505/507/509/511 [M-H]-	1
A805	H	H	2,4-di-Cl	3-CO2H	377/379/381	1
A806	H	H	2,4-di-Cl	3-OMe	363/365/367	1
A807	H	H	2,4-di-Cl	3,4-[OCH2O]	375/377/379[M-H]-	1
A808	H	H	3-Cl	3,5-di-Cl-4-OH	381/383/385/387[M-H]-	1
A809	H	H	3-Cl	3-CO2H	343/345	1
A810	H	H	3-Cl	3-OMe	329/331	1
A811	H	H	3-Cl-4-OMe	3,4-[OCH2O]	373/375	1

A812	H	H	3-Br	3,5-di-Cl-4-OH	425/427/429/431[M-H]-	1
A813	H	H	4-SMe	3,5-di-Cl-4-OH	393/395/397 [M-H]-	1
A814	H	H	4-F	3,5-di-Cl-4-OH	365/367/369 [M-H]-	1
A815	H	H	3-Cl	3,4-[OCH2O]	343/345	1
A816	H	H	4-Cl	3,4-[CO(CH2)4]	381/383	1
A817	H	H	4-Cl	3,4-[CH2SO2CH2]	387/389[M-H]-	1
A818	H	H	4-Cl	3,4-[O-C(Me)=N]	354/356	1
A819	H	H	4-Cl	3,4-[OCF2O]	379/381	1
A820	H	H	4-Cl	3,4-[O(CH2)3O]	371/373	1
A821	H	H	2,3-di-F	3,5-di-Cl-4-OH	383/385/387[M-H]-	1
A822	H	H	2,6-di-Cl	3,5-di-Cl-4-OH	415/417/419/421/423 [M-H]-	1
A823	H	H	3,4-di-Cl	3,5-di-Cl-4-OH	415/417/419/421/423 [M-H]-	1
A824	H	H	2-F	3,5-di-Cl-4-OH	367/369/371	1
A825	H	H	2-Me	3,5-di-Cl-4-OH	363/365/367	1
A826	H	H	4-NO2	3,5-di-Cl-4-OH	392/394/396 [M-H]-	1
A827	H	H	3-OPh	3,5-di-Cl-4-OH	441/443/445	1
A828	H	H	4-OPh	3,5-di-Cl-4-OH	441/443/445	1
A829	H	H	3-NO2-4-Cl	3,5-di-Cl-4-OH	426/428/430/432 [M-H]-	1
A830	H	H	4-OH	3-Cl-4-OH	331/333	4
A831	H	H	4-OH	3-Br-4-OH	375/377	4
A832	H	H	4-Cl	4-*trans*-CH=CHCO2H	369/371	13
A833	H	H	4-Cl	4-*trans*-	368/370	14

WO 00/21927 PCT/GB99/03280

				CH=CHCONH2		
A834	H	Me	4-Cl	4-OMe	343/345	1
A835	H	H	3,4,5-tri-F	3,5-di-Cl-4-OH	401/403/405 [M-H]-	1
A836	H	H	2-NO2	3,5-di-Cl-4-OH	392/395/397 [M-H]-	1
A837	H	H	3,5-di-F	3,5-di-Cl-4-OH	383/385/387 [M-H]-	1
A838	H	H	4-Cl	3-[OC6F5]	481/483	1
A839	H	H	4-Cl	2,3-[OCF2O]	377/379[M-H]-	1
A840	H	H	2-F	3,4-[S-CH=N]	340	1
A841	H	H	3-F	3,4-[S-CH=N]	340	1
A842	H	H	3-Cl	3,4-[S-CH=N]	356/358	1
A843	H	H	4-CF3	3,5-di-Cl-4-OH	415/417/419 [M-H]-	1
A844	H	H	3-SCF3	3,5-di-Cl-4-OH	447/449/451 [M-H]-	1
A845	H	H	4-OCF3	3,5-di-Cl-4-OH	431/433/435 [M-H]-	1
A846	H	H	3-CF3	3,5-di-Cl-4-OH	415/417/419 [M-H]-	1
A847	H	H	3,5-bis-CF3	3,5-di-Cl-4-OH	483/485/487 [M-H]-	1
A848	H	H	3,4-[OCH2O]	3,5-di-Cl-4-OH	393/395/397	1
A849	H	H	2-OCH2Ph	3,5-di-Cl-4-OH	455/457/459	1
A850	H	H	3,4-[(-CH=CH-)2]	3,5-di-Cl-4-OH	399/401/403	1
A851	H	H	4-Cl	3,4-[N=C(Me)-O]	354/356	1
A852	H	H	4-F	3,4-[S-CH=N]	340	1
A853	H	H	3-Br	3,4-[S-CH=N]	400/402	1
A854	H	H	2-Br	3,4-[S-CH=N]	400/402	1
A855	Me	H	4-Cl	3-CO2H-4-Cl	389/391/393 [M-H]-	1
A856	Me	H	4-Cl	4-CH2SO2NHMe	420/422	1
A857	Me	H	4-Cl	3,5-di-F	349/351	1
A858	Me	H	4-Cl	3,4-[OCH2O]	357/359	1

A859	Me	H	4-Cl	3,5-di-Cl-4-OH	397/399/401/403	1
A860	Me	H	4-Cl	4-(CH2)2CO2Me	399/401	1
A861	Me	H	4-Cl	4-(CH2)2CO2H	385/387	1
A862	H	H	4-COPh	3,5-di-Cl-4-OH	453/455/457	1
A863	H	H	3,4-di-F	4-SMe	347	1
A864	H	H	3,4-di-F	3,4-[(CH2)3]	341	1
A865	H	H	2,4-di-Cl	3,4-[S-CH=N]	390/392/394	1
A866	H	H	3,4-di-Cl	3,4-[S-CH=N]	390/392/394	1
A867	H	H	3-F	3,5-di-F	317 [M-H]-	1
A868	H	H	3-F	4-CH2SO2NHMe	390	1
A869	H	H	3-F	4-(CH2)2CO2H	355	1
A870	H	H	3-F	3-OMe	313	1
A871	H	H	3-F	3-Cl	317/319	1
A872	H	H	3-F	3-Cl-4-OMe	347/349	1
A873	H	H	3-F	3-Cl-4-OH	333/335	1
A874	H	H	3-F	4-(CH2)3CO2H	367 [M-H]-	1
A875	H	H	3-F	3,5-di-Me	311	1
A876	H	H	3-F	3-Cl-4-Me	331/333	1
A877	H	H	3-F	H	283	1
A878	H	H	2-Cl	3-F	315/317 [M-H]-	1
A879	H	H	2-Cl	3-OMe	329/331	1
A880	H	H	2-Cl	3-Cl-4-OMe	363/365/367	1
A881	H	H	2-Cl	3-Cl-4-OH	349/351/353	1
A882	H	H	2-Cl	4-(CH2)3CO2H	385/387	1
A883	H	H	2-Cl	3,5-di-OMe	359/361	1
A884	H	H	2-Cl	3-NO2-4-OH	360/362	1

A885	H	H	2-Cl	4-CH2P(O)(OEt)2	449/451	1
A886	H	H	2-Cl	4-NHCOMe	356/358	1
A887	H	H	2-Cl	4-(CH2)2CONH2	370/372	1
A888	H	H	2-Cl	3-CH2OH	329/331	1
A889	H	H	4-Cl	3-Cl-4-OMe	363/365/367	1
A890	H	H	4-Cl	3-Cl-4-OH	349/351/353	1
A891	H	H	4-Cl	3-CN	322/324 [M-H]-	1
A892	H	H	4-Cl	3-CO2Me	357/359	1
A893	H	H	4-Cl	2-Me-5-CO2Me	371/373	1
A894	H	H	4-Cl	3-Cl-4-Me	347/349/351	1
A895	H	H	3,4-di-F	3-CO2Me	359	1
A896	H	H	3,4-di-F	3-CO2H	343 [M-H]-	1
A897	H	H	4-Cl	2,3-[S-CH=N]	356/358	1
A898	H	H	4-Cl	3,4-[N=CH-S]	356/358	1
A899	H	H	4-Cl	3,4-[(CH2)2N(COMe)]	380/382[M-H]-	1
A900	H	H	4-Cl	3,4-[N(COMe)(CH2)2]	380/382[M-H]-	1
A901	H	H	3,4-di-F	3,4-[S-CH=N]	358	1
A902	H	H	4-Cl	3,4-[CH=CHCO-O]	367/369	1
A903	H	H	2-Cl	4-CH2NHCONHPh	445/447 [M-H]-	1
A904	H	H	4-Cl	4-OCH2CO2Me	385/387 [M-H]-	1
A905	H	H	2-Cl	4-(CH2)2CO2H	371/373	1
A906	H	H	2,6-di-Cl	3,4-[S-CH=N]	390/392/394	1
A907	H	H	3-Cl	3-CO2H-4-Cl	377/379/381	1
A908	H	H	3-Cl	3-Cl-4-OH	349/351/353	1

A909	H	H	3-Cl	3,5-di-F	335/337	1
A910	H	H	3-Cl	3-CH2OH	329/331	1
A911	H	H	3-Cl	3-OH	315/317	1
A912	H	H	3-Cl	4-CH2SO2NHMe	406/408	1
A913	H	H	2,4-di-OMe	3,5-di-Cl-4-OH	407/409/411 [M-H]-	13
A914	H	H	2-OEt	3,5-di-Cl-4-OH	391/393/395 [M-H]-	13
A915	H	H	4-OnBu	3,5-di-Cl-4-OH	419/421/423 [M-H]-	13
A916	H	H	3,4,5-tri-OMe	3,5-di-Cl-4-OH	439/441/443	13
A917	H	H	2-OPh	3,5-di-Cl-4-OH	441/443/445	13
A918	H	H	4-Ph	3,5-di-Cl-4-OH	425/427/429	13
A919	H	H	2-OMe-5-Br	3,5-di-Cl-4-OH	457/459/461	13
A920	H	H	4-Cl	4-CH2NHCONHPh	445/447 [M-H]-	1
A921	H	H	4-Cl	3-CO2Me-4-Cl	391/393/395	1
A922	H	H	2,3-di-F	3-CO2H-4-Cl	379/381	1
A923	H	H	3,4,5-tri-F	3-CO2H-4-Cl	395/397 [M-H]-	1
A924	H	H	3,5-di-F	3-CO2H-4-Cl	377/379 [M-H]-	1
A925	H	H	2-NO2	3-CO2H-4-Cl	388/390	1
A926	H	H	3,4-di-F	3-CO2H-4-Cl	377/379 [M-H]-	1
A927	H	H	2,3-di-F	3,4-[OCH2O]	345	1
A928	H	H	3,4,5-tri-F	3,4-[OCH2O]	363	1
A929	H	H	2,3-di-F	3,5-di-F	337	22
A930	H	H	2-F	3-CH2OH	313	1
A931	H	H	2,3-di-F	3-CH2OH	331	1
A932	H	H	3,4,5-tri-F	3-CH2OH	349	1
A933	H	H	3,5-di-F	3-CH2OH	331	1
A934	H	H	2-NO2	3-CH2OH	338 [M-H]-	1

A935	H	H	3,4-di-F	3-CH2OH	331	1
A936	H	H	2-OPh	3-CH2OH	387	1
A937	H	H	2,4-di-Cl	3-CH2OH	363/365/367	1
A938	H	H	2,3-di-F	3-OH	317	1
A939	H	H	3,5-di-F	3-OH	317	1
A940	H	H	2,3-[(-CH=CH-)2]	3,5-di-Cl-4-OH	399/401/403	13
A941	H	H	4-Cl	4-SCH2CO2H	389/391	13
A942	H	H	4-Cl	3,4-[O(CH2)2O]	357/359	1
A943	H	H	3,4-di-Cl	3-CO2H-4-Cl	409/411/413/415 [M-H]-	1
A944	H	H	3,4-di-Cl	3-Cl-4-OH	383/385/387/389	1
A945	H	H	3,4-di-Cl	3,5-di-F	367/369/371 [M-H]-	1
A946	H	H	3,4-di-Cl	3-CH2OH	363/365/367	1
A947	H	H	3,4-di-Cl	3-OH	349/351/353	1
A948	H	H	3,4-di-Cl	4-CH2SO2NHMe	438/440/442 [M-H]-	1
A949	H	H	4-SO2Me	3-CO2H-4-Cl	419/421 [M-H]-	1
A950	H	H	4-SO2Me	3,4-[OCH2O]	386 [M]-	1
A951	H	H	4-SO2Me	3-Cl-4-OH	391/393 [M-H]-	1
A952	H	H	4-SO2Me	3,5-di-F	379	1
A953	H	H	2-OMe-5-Br	3-CO2H-4-Cl	451/453/455	1
A954	H	H	2-OMe-5-Br	3,4-[OCH2O]	417/419	1
A955	H	H	2-OMe-5-Br	3-Cl-4-OH	423/425/427	1
A956	H	H	2-OMe-5-Br	3,5-di-F	409/411	1
A957	H	H	2-OMe-5-Br	3-CH2OH	403/405	1
A958	H	H	2-OMe-5-Br	3-OH	389/391	1
A959	H	H	2-Me	3,4-[OCH2O]	323	1

A960	H	H	2-Me	3-Cl-4-OH	329/331	1
A961	H	H	2-Me	3-CH2OH	309	1
A962	H	H	2-Me	3-OH	295	1
A963	H	H	3-Br	3-CO2H-4-Cl	419/421/423 [M-H]-	1
A964	H	H	3-Br	3,4-[OCH2O]	387/389	1
A965	H	H	3-Br	3-Cl-4-OH	393/395/397	1
A966	H	H	3-Br	3,5-di-F	379/381	1
A967	H	H	4-Cl	4-*trans*-CH=CHPh	401/403	1
A968	H	H	4-Cl	4-SCH2CO-NH(CH2)2OMe	446/448	17
A969	H	H	2-F	3-CO2H-4-Cl	361/363	1
A970	H	H	2,4-di-Cl	3-CO2H-4-Cl	411/413/415/417	1
A971	H	H	2-F	3,4-[OCH2O]	327	1
A972	H	H	3,5-di-F	3,4-[OCH2O]	345	1
A973	H	H	2-NO2	3,4-[OCH2O]	354	1
A974	H	H	3,4-di-F	3,4-[OCH2O]	345	1
A975	H	H	2-OPh	3,4-[OCH2O]	401	1
A976	H	H	3,4-di-Cl	3,4-[OCH2O]	377/379/381	1
A977	H	H	2-F	3-Cl-4-OH	333/335	1
A978	H	H	2,3-di-F	3-Cl-4-OH	351/353	1
A979	H	H	3,4,5-tri-F	3-Cl-4-OH	369/371	1
A980	H	H	3,5-di-F	3-Cl-4-OH	351/353	1
A981	H	H	2-NO2	3-Cl-4-OH	360/362	1
A982	H	H	3,4-di-F	3-Cl-4-OH	351/353	1
A983	H	H	2-OPh	3-Cl-4-OH	407/409	1
A984	H	H	2,4-di-Cl	3-Cl-4-OH	383/385/387/389	1

A985	H	H	2-F	3,5-di-F	319	1
A986	H	H	3,4,5-tri-F	3,5-di-F	353 [M-H]-	1
A987	H	H	3,5-di-F	3,5-di-F	335 [M-H]-	1
A988	H	H	3,4-di-F	3,5-di-F	335 [M-H]-	1
A989	H	H	2-F	3-OH	299	1
A990	H	H	3,4,5-tri-F	3-OH	335	1
A991	H	H	2-NO2	3-OH	326	1
A992	H	H	3,4-di-F	3-OH	317	1
A993	H	H	2-OPh	3-OH	373	1
A994	H	H	2,4-di-Cl	3-OH	349/351/352	1
A995	H	H	4-Br	4-SO2NH2	420/422 [M-H]-	3
A996	H	H	4-Cl	3-SO2NH*n*Bu	434/436	1
A997	H	H	4-Cl	2,3-[N=CH-CH=CH]	350/352	13
A998	H	H	2-OEt	3-Cl	343/345	
A999	H	H	2-OPh	3-Cl	391/393	
A1000	H	H	2-OMe-5-Br	3-Cl	405/407/409 [M-H]-	
A1001	H	H	3-F	3-SO2NH*n*Bu	418	1
A1002	H	H	4-Cl	2-Me-5-CO2H	355/357 [M-H]-	13
A1003	H	H	2-Cl	3-CH2CO2H	357/359	13
A1004	H	H	4-Cl	2-OH-5-CO2H	359/361	13
A1005	H	H	2-F-6-Cl	H	317/319	1
A1006	H	H	2-F-6-Cl	3-Br	395/397/399	1
A1007	H	H	2-F-6-Cl	4-SMe	363/365	1
A1008	H	H	2-F-6-Cl	4-Me	331/333	1
A1009	H	H	2-F-6-Cl	3,4-[OCH2O]	361/363	1
A1010	H	H	2-F-6-Cl	3,4-[(CH2)3]	357/359	1

A1011	H	H	2-F-6-Cl	4-CH2SO2NHMe	424/426	1
A1012	H	H	4-I	H	391	1
A1013	H	H	3-F	2-Me	297	1
A1014	H	H	3-F	3-Me	297	1
A1015	H	H	3-F	3-CH2OH	313	1
A1016	H	H	3-F	3-F	301	1
A1017	H	H	3-F	3,5-di-OMe	343	1
A1018	H	H	3-F	3,5-di-Br-4-Me	453/455/457	1
A1019	H	H	3-F	4-CH2P(O)(OEt)2	433	1
A1020	H	H	3-F	4-F	301	1
A1021	H	H	3-F	4-OMe	313	1
A1022	H	H	3-F	4-CH2NHCOPh	416	13
A1023	H	H	3-F	4-CH2NHCOMe	354	13
A1024	H	H	4-Cl	4-CH2NHCOMe	368/370 [M-H]-	13
A1025	H	H	2,6-di-F	3,5-di-Cl-4-OH	385/387/389	13
A1026	H	H	4-I	4-CH2SO2NHMe	498	1
A1027	H	H	2,5-di-Me	3,5-di-Cl-4-OH	375/377/379 {M-H]-	13
A1028	H	H	2-F-6-Cl	3,5-di-Cl-4-OH	399/401/403/405 [M-H]-	13
A1029	H	H	2-OCF3	3,5-di-Cl-4-OH	431/433/435 [M-H]-	13
A1030	H	H	3-F	3-CN	306 [M-H]-	1
A1031	H	H	3-F	3,4-di-Cl	351/353/355	1
A1032	H	H	4-I	4-Me	403 [M-H]-	1
A1033	H	H	4-I	3-[*trans*-CH=CHCONMe2]-4-Cl	522/524	1

A1034	H	H	3-F	3-[*trans*-CH=CHCONMe2]-4-Cl	412/414 [M-H]-	1
A1035	H	H	3-F	2-F	301	1
A1036	H	H	3-F	2-Me-5-Cl	331/333	1
A1037	H	H	3-F	2-Me-4-OMe	327	1
A1038	H	H	3-F	3-COPh	387	1
A1039	H	H	3-F	3-COMe	325	1
A1040	H	H	3-F	4-(CH2)2CONH2	354	1
A1041	H	H	2,6-di-F	3-Cl	335/337	1
A1042	H	H	2-F-6-Cl	3-Cl	351/353/355	1
A1043	H	H	2,5-di-F	3-Cl	335/337	1
A1044	H	H	2,5-di-Me	3-Cl	327/329	1
A1045	H	H	2-I	3-Cl	425/427	1
A1046	H	H	2-OCF3	3-Cl	383/385	1
A1047	H	H	2-F-6-Cl	4-(CH2)2CONH2	388/390	1
A1048	H	H	4-I	3,5-di-Cl	457/459/461 [M-H]-	1
A1049	H	H	4-I	4-(CH2)2CONH2	462	1
A1050	H	H	3-F	4-OPh	375	1
A1051	H	H	4-I	3,5-di-Cl-4-OH	347/349/351 [M-I]-	13
A1052	H	H	3-F	4-(CH2)2NHCOPh	430	13
A1053	H	H	3-F	3-[4-Methylpiperazin-1-yl]-4-OMe	411	20
A1054	H	H	3-F	3,5-di-Cl-4-Me	363/365/367 [M-H]-	1
A1055	H	H	2,3-di-F	3,5-di-Cl-4-Me	383/385/387	1
A1056	H	H	4-Br	3,5-di-Cl-4-Me	425/427/429/431	1

A1057	H	H	2,5-di-F	3-Br	379/381	1
A1058	H	H	2-OCF3	3-Br	427/429	1
A1059	H	H	2,5-di-Me	4-Me	307	1
A1060	H	H	2-I	4-Me	405	1
A1061	H	H	2-OCF3	4-Me	363	1
A1062	H	H	4-I	3,5-di-Cl-4-Me	473/475/477	1
A1063	H	H	2-Cl	3,5-di-Cl-4-Me	381/383/385/387	1
A1064	H	H	3-Me	3,5-di-Cl-4-Me	361/363/365	1
A1065	H	H	2,4-di-Cl	3,5-di-Cl-4-Me	415/417/419/421/423	1
A1066	H	H	2-I	3-Br	469/471	1
A1067	H	H	2,6-di-F	3-Br	379/381	1
A1068	H	H	2,5-di-F	4-SMe	347	1
A1069	H	H	2,5-di-Me	4-SMe	339	1
A1070	H	H	2-I	4-SMe	437	1
A1071	H	H	2-OCF3	4-SMe	395	1
A1072	H	H	2,6-di-F	4-SMe	347	1
A1073	H	H	2,5-di-F	4-Me	315	1
A1074	H	H	2,6-di-F	4-Me	315	1
A1075	H	H	2,5-di-F	3,4-[OCH2O]	345	1
A1076	H	H	2,5-di-Me	3,4-[OCH2O]	337	1
A1077	H	H	2-I	3,4-[OCH2O]	435	1
A1078	H	H	2-OCF3	3,4-[OCH2O]	393	1
A1079	H	H	2,5-di-F	3,4-[(CH2)3]	341	1
A1080	H	H	2,5-di-Me	3,4-[(CH2)3]	333	1
A1081	H	H	2-I	3,4-[(CH2)3]	431	1
A1082	H	H	2-OCF3	3,4-[(CH2)3]	389	1

A1083	H	H	2,6-di-F	3,4-[(CH2)3]	341	1
A1084	H	H	2-OCF3	4-(CH2)2CONH2	420	1
A1085	H	H	2,5-di-F	H	301	1
A1086	H	H	2,5-di-Me	H	293	1
A1087	H	H	2-I	H	391	1
A1088	H	H	2-OCF3	H	349	1
A1089	H	H	2,6-di-F	H	301	1
A1090	H	H	2,3-di-F	3-CH2CONH2	358	1
A1091	H	H	2,3-di-F	3-CH2CONHMe	372	1
A1092	H	H	2,3-di-F	3-CONHMe	358	1
A1093	H	H	2,3-di-F	3-CONH2-4-Me	358	1
A1094	H	H	2,3-di-F	3-CONH(CH2)2OMe	402	1
A1095	H	H	3-F	3-CH2CONH2	340	1
A1096	H	H	3-F	3-CH2CONHMe	354	1
A1097	H	H	3-F	3-CONHMe	340	1
A1098	H	H	3-F	3-CONH2-4-Me	340	1
A1099	H	H	3-F	3-CONH(CH2)2OMe	384	1
A1100	H	H	3-F	3-CF3	351	1
A1101	H	H	3-F	4-*n*Bu	339	1
A1102	H	H	3-F	4-O*n*Bu	355	1
A1103	H	H	3-F	2-Et	311	1
A1104	H	H	3-F	2-*i*Pr	325	1
A1105	H	H	3-F	3,4-[OCF2O]	363	1
A1106	H	H	3-F	3,4-[(CH2)2N(COMe)]	366	1
A1107	H	H	3-F	3,4-[O(CH2)3O]	355	1

A1108	H	H	3-F	3,4-di-Me	311	1
A1109	H	H	3-F	3,4-di-OMe	343	1
A1110	H	H	3-F	3-Br-4-OCF3	445/447	1
A1111	H	H	3-F	3-CO2Me	341	1
A1112	H	H	3-F	3-CONH2	326	1
A1113	H	H	3-F	3-F-4-Me	315	1
A1114	H	H	3-F	3-I	409	1
A1115	H	H	3-F	3-OCH2Ph	389	1
A1116	H	H	3-F	4-CH2NHBOC	410 [M-H]-	1
A1117	H	H	3-F	4-Cl	317/319	1
A1118	H	H	3-F	4-NHCOMe	340	1
A1119	H	H	3-F	4-OCH2Ph	389	1
A1120	H	H	3-F	4-*t*Bu	339	1
A1121	H	H	3-F	2,3-[OCF2O]	363	1
A1122	H	H	3-F	2-Me-3-Br	375/377	1
A1123	H	H	3-F	2-Me-3-Cl	331/333	1
A1124	H	H	3-F	2-Me-5-CH2OH	325 [M-H]-	1
A1125	H	H	3-F	2-OPh	375	1
A1126	H	H	3-F	3,4-[CH2SO2CH2]	373	1
A1127	H	H	3-F	3-Br-4-Cl	395/397/399	1
A1128	H	H	3-F	3-O*i*Pr	341	1
A1129	H	H	3-F	3-SO2CF3	413 [M-H]-	1
A1130	H	H	3-F	2,3-di-Me	311	1
A1131	H	H	3-F	2,4-di-Me	311	1
A1132	H	H	3-F	2-Me-4-Cl	331/333	1
A1133	H	H	3-F	2-OMe	313	1

A1134	H	H	3-F	2-Ph	359	1
A1135	H	H	3-F	2-SMe	329	1
A1136	H	H	3-F	3-Et	311	1
A1137	H	H	2,5-di-Me	4-(CH2)2CONH2	364	1
A1138	H	H	2,5-di-F	4-(CH2)2CONH2	372	1
A1139	H	H	2-I	4-(CH2)2CONH2	462	1
A1140	H	H	2,6-di-F	4-(CH2)2CONH2	372	1
A1141	H	H	2,6-di-F	3,4-[OCH2O]	345	1
A1142	H	H	3,5-di-F	3,5-di-Cl-4-Me	383/385/387	1
A1143	H	H	2,5-di-F	4-CH2SO2NHMe	408	1
A1144	H	H	2,5-di-Me	4-CH2SO2NHMe	400	1
A1145	H	H	2-I	4-CH2SO2NHMe	498	1
A1146	H	H	2-OCF3	4-CH2SO2NHMe	456	1
A1147	H	H	2,6-di-F	4-CH2SO2NHMe	408	1
A1148	H	H	4-Cl	4-CH2NHCOPh	432/434	13
A1149	H	H	2,3-di-F	3,4-[S-CH=N]	358	1
A1150	H	H	4-Cl	4-*trans*-CH=CH-(4-OH-Ph)	417/419	1
A1151	H	H	4-I	4-Cl	425/427	1
A1152	H	H	4-I	4-OMe	421	1
A1153	H	H	3-F	4-*trans*-CH=CHCONH2	352	13
A1154	H	H	2,3-di-F	4-*trans*-CH=CHCONH2	370	13
A1155	H	H	3-F	3-[4-(COCHCl2)-Piperazin-1-yl]-4-OMe	507/509/511	13

A1156	H	H	3-F	4-*trans*-CH=CH-(4-OH-Ph)	401	1
A1157	H	H	3-F	4-[1,2,3-Thiadiazol-4-yl]	367	1
A1158	H	H	3-F	3-[O-(Pyrimidin-2-yl)]	377	13
A1159	H	H	3-F	4-[N(Me)(Pyrimidin-2-yl)]	390	20
A1160	H	H	3-F	3,4-[S-C(Me)=N]	354	1
A1161	H	H	3-F	3,4-[O-C(NHMe)=N]	353	1
A1162	H	H	2,3-di-F	4-[Morpholin-1-yl]	386	1
A1163	H	H	2,3-di-F	3,4-[OC(NHMe)=N]	371	13
A1164	H	H	3-F	3,4-[OC(=O)NH]	340	13
A1165	H	H	3-F	3-(CH2OH)-4-OMe	341 [M-H]-	13
A1166	H	H	3-F	3-(CH2NMe2)-4-OMe	370	13
A1167	H	H	2,3-di-F	3-Cl	335/337	1
A1168	H	(CH2)2OH	2,3-di-F	H	345	1
A1169	H	H	2,3-di-F	4-CH2SO2NHMe	408	1
A1170	H	H	2,3-di-F	3-CH2CO2H	359	13
A1171	H	H	2,3-di-F	4-CH2CO2H	359	13
A1172	H	H	2,3-di-F	4-OCH2CO2H	375	13
A1173	H	H	2,3-di-F	4-(CH2)2CO2H	373	13
A1174	H	H	2,3-di-F	4-(CH2)3CO2H	385 [M-H]-	13
A1175	H	H	2,3-di-F	4-NMe2	344	1
A1176	H	H	2,3-di-F	2,4-di-F	337	1
A1177	H	H	2,3-di-F	3,4-di-F	337	1

A1178	H	H	2,3-di-F	2,3-di-F	337	1
A1179	H	H	2,3-di-F	2,5-di-F	337	1
A1180	H	H	2,3-di-F	4-SPh	409	1
A1181	H	H	2,3-di-F	4-OPh	393	1
A1182	H	H	2,3-di-F	4-NHPh	392	1
A1183	H	H	2,3-di-F	2-OMe-3-F	349	1
A1184	H	H	2,3-di-F	3-Cl-4-Me	349/351	1
A1185	H	H	2,3-di-F	4-NHSO2Me	394	1
A1186	H	H	2,3-di-F	3-[CH2-(1,3-Thiazolidine-2,4-dion-5-yl)]	430	1
A1187	H	H	3-F	4-[OCH2-(1-Methyl-piperazin-4-yl)]	410	1
A1188	H	(CH2)2OH	2-Cl	H	343/345	3
A1189	H	(CH2)2OH	3,5-di-Me	H	337	3
A1190	H	H	2,3-di-F	3,4-[N=N-NH]	342	1
A1191	H	H	2,3-di-F	3,4-[CH=N-NH]	341	1
A1192	H	H	2,3-di-F	3,4-[NH-N=CH]	341	1
A1193	H	H	2,3-di-F	3,4-[OCF2O]	379 [M-H]-	1
A1194	H	H	2,3-di-F	3,5-di-Cl	367/369/371 [M-H]-	1
A1195	H	H	2,3-di-F	3,5-di-Me	327 [M-H]-	1
A1196	H	H	2,3-di-F	2-F	317 [M-H]-	1
A1197	H	H	2,3-di-F	3-Cl-4-OMe	363/365 [M-H]-	1
A1198	H	H	2,3-di-F	3-CO2H	343 [M-H]-	1

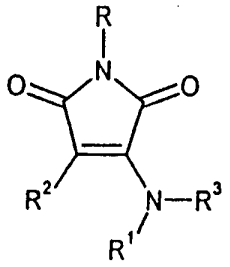
A1199	H	H	2,3-di-F	3-F	319	1
A1200	H	H	2,3-di-F	3-F-4-Me	333	1
A1201	H	H	2,3-di-F	3-I	425 [M-H]-	1
A1202	H	H	2,3-di-F	3-OMe	329 [M-H]-	1
A1203	H	H	2,3-di-F	4-CH2CH2CONH2	370 [M-H]-	1
A1204	H	H	2,3-di-F	4-F	317 [M-H]-	1
A1205	H	H	2,3-di-F	4-Cl	333/335 [M-H]-	1
A1206	H	H	2,3-di-F	4-NHCOMe	358	1
A1207	H	H	2,3-di-F	4-OMe	331	1
A1208	H	H	2,3-di-F	4-CH2CONH2	358	1
A1209	H	H	2,3-di-F	3-CH2OMe	343 [M-H]-	1
A1210	H	H	2,3-di-F	3-CH(OH)Ph	405 [M-H]-	1
A1211	H	H	3,5-di-Cl	4-CH2SO2NHMe	438/440/442 [M-H]-	1
A1212	H	H	3,5-di-Cl	4-CH2CH2CONH2	402/404/406 [M-H]-	1
A1213	H	H	3,5-di-Cl	3,5-di-F	367/369/371 [M-H]-	1
A1214	H	H	3,5-di-Cl	4-Me	345/347/349 [M-H]-	1
A1215	H	H	3,5-di-Cl	3-Cl	365/367/369/371 [M-H]-	1
A1216	H	H	3,5-di-Cl	H	331/333/335 [M-H]-	1
A1217	H	H	2,3,5-tri-F	4-CH2SO2NHMe	424 [M-H]-	1
A1218	H	H	2,3,5-tri-F	4-CH2CH2CONH2	390	1
A1219	H	H	2,3,5-tri-F	3,5-di-F	353 [M-H]-	1
A1220	H	H	2,3,5-tri-F	4-Me	333	1
A1221	H	H	2,3,5-tri-F	3-Cl	351/353 [M-H]-	1
A1222	H	H	2,3,5-tri-F	3,4-[(CH2)3]	359	1
A1223	H	H	2,3,5-tri-F	H	319	1

A1224	H	H	2,3-di-F	3,4-[O(CH2)3O]	373	1
A1225	H	H	2,3-di-F	3-F-4-OMe	349	1
A1226	H	H	2,3-di-F	4-(CH2)2OH	345	1
A1227	H	H	2,3-di-F	4-CH2CN	340	1
A1228	H	H	3,5-di-Cl	3,4-[(CH2)3]	371/373/375 [M-H]-	1
A1229	H	H	2,3-di-F	3-[CO2H]-4-[CH2CO2H]	401	1
A1230	H	H	2,3-di-F	4-[4-Methyl-piperazin-1-yl]	399	20
A1231	H	H	2,3-di-F	3,4-[O(CH2)2O]	357 [M-H]-	1
A1232	H	H	2,3-di-F	4-[CH2CO-(Morpholin-1-yl)]	426 [M-H]-	1
A1233	H	H	2,3-di-F	4-[CH2CONH(CH2)2OMe]	416	1
A1234	H	H	3-NO2	4-[(CH2)2CONH(CH2)6NHBOC]	578 [M-H]-	12
A1235	H	H	3-NO2	4-[(CH2)2CONH(CH2)6NH2]	480	10
A1236	H	H	3-NO2	4-[(CH2)2CONH(CH2)6NH-Biotinyl]	706	9
A1237	H	H	2,3-di-F	3-[CH2CH(Me)CO2H]	385 [M-H]-	13

A1238	H	H	2,3,5-tri-F	3,5-di-Cl-4-OH	401/403/405 [M-H]-	13
A1239	H	H	3,5-di-Cl	3,5-di-Cl-4-OH	415/417/419/421/423 [M-H]-	13
A1240	H	H	3,5-di-F	2,3-di-F	337	1
A1241	H	H	2,3-di-F	4-[SCH2CO2H]	391	13

Table B

Encompassing compounds of general formula (I) and substituents R, R^1, R^2 and R^3 are listed in Table B.



(I)

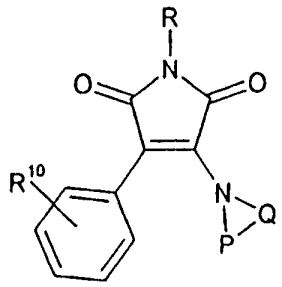
Example No.	R	R^1	R^2	R^3	$[M+H]^+$ Observed; (Unless $[M]^-$ or $[M-H]^-$ are Indicated)	For Procedure See Example No.
B1	Me	Me	Indol-3-yl	Ph	332	3
B2	H	H	Indol-3-yl	H	228	5
B3	H	Me	Indol-3-yl	Ph	318	5
B4	H	H	Ph	H	189	1
B5	H	H	Ph	CH2Ph	279	1
B6	CH2Ph	H	Ph	CH2Ph	369	1

B7	H	Et	4-CF3-Ph	Et	313	1
B8	H	Me	4-OMe-Ph	CH2Ph	323	1
B9	H	Et	4-Cl-Ph	Et	279/281	1
B10	H	Me	4-Cl-Ph	CH2Ph	327/329	1
B11	H	Me	4-Cl-Ph	(CH2)2Ph	341/343	1
B12	H	Et	Ph	Et	245	1
B13	H	Me	Ph	CH2Ph	293	1
B14	H	Me	Ph	(CH2)2Ph	307	1
B15	H	(CH2)2OMe	4-Cl-Ph	(CH2)2OMe	339/341	1
B16	H	H	3-NO2-Ph	4-Me-Oxazol-2-yl	315	1
B17	H	Me	3-NO2-Ph	CH2Ph	338	1
B18	H	Me	3-NO2-Ph	(CH2)2Ph	352	1
B19	H	H	3-NO2-Ph	Cyclohexyl	314 [M-H]-	1
B20	H	H	2-OMe-Ph	Fluoren-2-yl	383	1
B21	H	H	3-NO2-Ph	Fluoren-2-yl	396 [M-H]-	1
B22	H	H	4-Cl-Ph	Dibenzofuran-2-yl	389/391	1
B23	H	H	4-Cl-Ph	Dibenzofuran-3-yl	389/391	1
B24	H	H	4-Cl-Ph	(2-Acetylbenzofuran-5-yl)	381/383	1
B25	H	H	3-NO2-Ph	H	234	16
B26	H	H	4-Cl-Ph	2,6-di-Me-pyridin-3-yl	328/330	13
B27	H	H	4-Cl-Ph	(CH2)2OMe	281/283	18
B28	H	H	4-I-Ph	(CH2)2OMe	373	18
B29	H	H	4-Cl-Ph	2-Methylpyridin-3-yl	314/316	13
B30	H	H	4-Cl-Ph	2-Chloropyridin-5-yl	332/334/336 [M-H]-	13

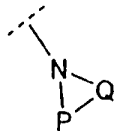
B31	H	H	4-Cl-Ph	Quinolin-3-yl	350/352	13
B32	H	H	4-Cl-Ph	Pyrimidin-2-yl	301/303	13
B33	Me	H	3-F-Ph	H	219 [M-H]-	16
B34	H	H	2,3-di-F-Ph	2,6-di-Me-pyridin-3-yl	330	13

Table C

Encompassing compounds of general formula (XXX-2), wherein group R^2 of formula (I) is a phenyl ring, optionally substituted by one or more substituents R^{10} and the moiety $-NR^1R^3$ of formula (I) represents a heterocyclyl moiety of general formula (XXX-3) and substituents R, R^{10} and P-Q are listed in Table C.



(XXX-2)



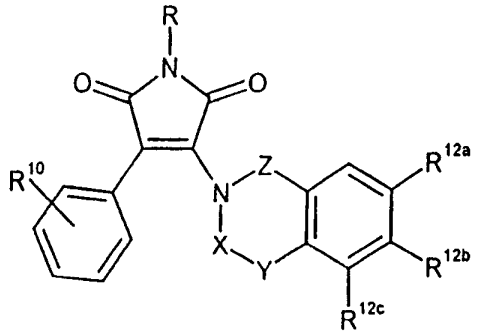
(XXX-3)

Example No.	R	R^{10}	P-Q	$[M+H]^+$ Observed; (Unless $[M]^-$ or $[M-H]^-$ are Indicated)	For Procedure See Example No.
C1	H	4-OMe	(CH2)2O(CH2)2	289	1
C2	H	4-Cl	(CH2)4	277/279	1
C3	H	4-Cl	(CH2)2O(CH2)2	293/295	1
C4	H	4-Cl	(CH2)3CH(Me)CH2	305/307	1
C5	H	4-Cl	(CH2)3CH(CONH2)CH2	332/334[M-H]-	1

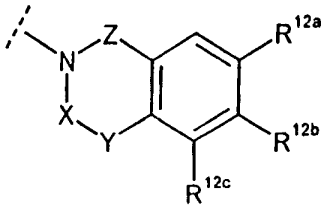
C6	H	H	(CH2)3CH(CONH2)CH2	300	1
C7	H	4-OMe	(CH2)3CH(CONH2)CH2	330	1
C8	H	H	(CH2)4	243	1
C9	H	4-Cl	(CH2)3CH(CH2OH)CH2	321/323	1
C10	H	4-Cl	(CH2)5	291/293	1
C11	H	4-Cl	(CH2)2CH(CH2Ph)(CH2)2	381/383	1
C12	H	4-Cl	(CH2)2CH(OH)(CH2)2	307/309	1
C13	H	3-NO2	(CH2)3CH(Me)CH2	316	1
C14	H	2,4-di-Cl	(CH2)5	325/327/329	1
C15	H	2,4-di-Cl	(CH2)2O(CH2)2	327/329/331	1
C16	H	2,4-di-Cl	(CH2)2S(CH2)2	341/343/345 [M-H]-	1

Table D

Encompassing compounds of general formula (XXX-4), wherein group R^2 of formula (I) is a phenyl ring, optionally substituted by one or more substituents R^{10} and the moiety $-NR^1R^3$ of formula (I) represents a heterocyclyl moiety of general formula (XXX-5), optionally substituted by substituents R^{12a}, R^{12b} and R^{12c} and substituents R, R^{10}, R^{12a}, R^{12b}, R^{12c};X-Y and Z are listed in Table D.



(XXX-4)



(XXX-5)

Example No.	R	R^{10}	R^{12a}	R^{12b}	R^{12c}	X-Y	Z	$[M+H]^+$ Observed; (Unless $[M]^-$ or $[M-H]^-$ are Indicated)	For Procedure See Example No.
D1	H	4-CF3	H	H	H	CH=N	bond	358	2
D2	H	4-Cl	H	H	H	(CH2)2	bond	325/327	1
D3	H	4-Cl	H	H	H	(CH2)2	CH2	339/341	1

D4	H	4-Cl	H	H	H	(CH2)3	bond	339/341	1
D5	H	4-Cl	NO2	H	H	(CH2)2	bond	370/372	1
D6	H	3-NO2	H	H	H	(CH2)2	CH2	350	1
D7	H	4-OMe	H	H	H	(CH2)2	bond	321	1
D8	H	4-Cl	H	H	H	(CH2)2	(CH2)2	353/355	1
D9	H	3-NO2	H	H	H	(CH2)2	(CH2)2	364	1
D10	H	3-CF3	H	H	H	(CH2)2	bond	359	1
D11	H	3,5-di-F	H	H	H	(CH2)2	bond	327	1
D12	H	3-NO2	H	H	H	(CH2)2	bond	336	1
D13	H	2-OMe	H	H	H	(CH2)2	bond	321	1
D14	H	2-Cl	H	H	H	(CH2)2	bond	325/327	1
D15	H	2-OMe	H	H	H	(CH2)2	CH2	335	1
D16	H	2-OMe	H	H	H	CH(Me)CH2	bond	335	1
D17	H	2-Cl	H	H	H	CH(Me)CH2	bond	339/341	1
D18	H	3,5-di-F	H	H	H	CH(Me)CH2	bond	341	1
D19	H	3-NO2	H	H	H	CH=CH	bond	334	15
D20	H	3-NO2	H	H	H	CH(CO2H)CH 2	bond	380	1
D21	H	3,4-di-F	H	H	H	(CH2)2	bond	327	1
D22	H	3-NO2	H	H	H	CH(CO2Me)C H2	bond	392 [M-H]-	1
D23	H	4-I	H	H	H	(CH2)2	bond	417	1
D24	H	3-Cl	H	H	H	(CH2)2	bond	325/327	1
D25	H	4-Br	H	H	H	(CH2)2	bond	369/371	1
D26	H	3-Br	H	H	H	(CH2)2	bond	369/371	1
D27	H	2-Me	H	H	H	(CH2)2	bond	305	1

D28	H	3-F	H	H	H	(CH2)2	bond	309	1
D29	H	2,4-di-Cl	H	H	H	(CH2)2	bond	359/361/363	1
D30	H	2-Br	H	H	H	(CH2)2	bond	369/371	1
D31	H	2-F	H	H	H	(CH2)2	bond	309	1
D32	H	4-COPh	H	H	H	(CH2)2	bond	394 [M]-	1
D33	H	2-NO2	H	H	H	(CH2)2	bond	336	1
D34	H	3,4,5-tri-F	H	H	H	(CH2)2	bond	343 [M-H]-	1
D35	H	2-OEt	H	H	H	(CH2)2	bond	335	1
D36	H	3-F	[4-Ethyl-piperazin-1-yl]	OMe	H	(CH2)2	bond	451	20
D37	H	3-F	H	H	H	CH(Me)CH2	bond	323	1
D38	H	2,3-di-F	H	H	H	CH(Me)CH2	bond	341	1
D39	H	2-F	H	H	H	CH(Me)CH2	bond	323	1
D40	H	2-Me	H	H	H	CH(Me)CH2	bond	319	1
D41	H	2-Br	H	H	H	CH(Me)CH2	bond	383/385	1
D42	H	4-OMe	H	H	H	CH(Me)CH2	bond	335	1
D43	H	4-Cl	H	H	H	CH(Me)CH2	bond	339/341	1
D44	H	4-I	H	H	H	CH(Me)CH2	bond	431	1
D45	H	3-Me	H	H	H	CH(Me)CH2	bond	319	1
D46	H	3,5-di-Me	H	H	H	CH(Me)CH2	bond	333	1
D47	H	3-F	H	H	H	(CH2)3	bond	323	1
D48	H	3-F	[4-(BOC)-Piperazin-1-yl]	OMe	H	(CH2)2	bond	521 [M-H]-	20
D49	H	3-F	[4-Me-	Cl	H	(CH2)2	bond	441/443	20

			Piperazin-1-yl]						
D50	H	3-F	[4-Me-Piperazin-1-yl]	Me	H	(CH2)2	bond	421	20
D51	H	2-Cl	H	H	H	CH(CH2OH)CH2	bond	355/357	1
D52	H	2-OMe	H	H	H	CH(CH2OH)CH2	bond	351	1
D53	H	3-F	H	H	H	CH(CH2OH)CH2	bond	339	1
D54	H	2,3-di-F	H	H	H	CH(CH2OH)CH2	bond	357	1
D55	H	3,5-di-F	H	H	H	CH(CH2OH)CH2	bond	357	1
D56	H	3,5-di-Me	H	H	H	CH(CH2OH)CH2	bond	349	1
D57	H	2-Cl	H	H	H	CH2CH(Me)	bond	339/341	1
D58	H	3-F	H	H	H	CH2CH(Me)	bond	323	1
D59	H	3-F	[Piperazin-1-yl]	OMe	H	(CH2)2	bond	421 [M-H]-	20
D60	H	2-Cl	H	H	H	CH2CH(CH2OH)	bond	355/357	20
D61	H	3-F	H	H	H	CH2CH(CH2OH)	bond	339	20
D62	H	2,3-di-F	H	H	H	CH2CH(CH2O	bond	357	20

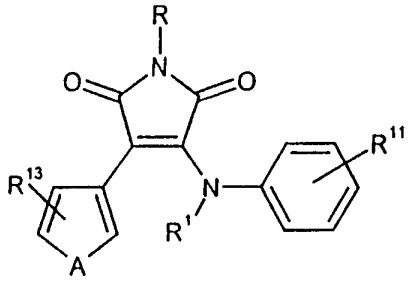
						H)			
D63	H	2,3-di-F	H	H	H	CH2	CH2	325 [M-H]-	20
D64	H	2,3-di-F	H	H	H	CH2C(Me2)	bond	355	1
D65	H	2,3-di-F	OMe	H	H	(CH2)2	bond	357	1
D66	H	2,3-di-F	H	Br	H	(CH2)2	bond	405/407	1
D67	H	2-Cl	H	H	H	CH2C(Me2)	bond	353/355	1
D68	H	2-Cl	H	F	H	(CH2)2	bond	343/345	1
D69	H	2,3-di-F	NO2	H	H	(CH2)2	bond	372	1
D70	H	3,5-di-Me	OMe	H	H	(CH2)2	bond	349	1
D71	H	2,3-di-F	H	H	H	CH2CH(Me)	bond	341	1
D72	H	2,3-di-F	OMe	OMe	H	(CH2)2	bond	387	1
D73	H	2,3-di-F	H	H	Br	(CH2)2	bond	405/407	1
D74	H	2,3-di-F	H	F	H	(CH2)2	bond	345	1
D75	H	2,3-di-F	F	H	H	(CH2)2	bond	345	1
D76	H	2,3-di-F	CF3	Me	H	(CH2)2	bond	409	1
D77	H	2,3-di-F	CF3	OMe	H	(CH2)2	bond	425	1
D78	H	2-Cl	OMe	H	H	(CH2)2	bond	355/357	1
D79	H	2-Cl	H	H	Br	(CH2)2	bond	403/405/407	1
D80	H	2-Cl	H	Br	H	(CH2)2	bond	403/405/407	1
D81	H	2-Cl	F	H	H	(CH2)2	bond	343/345	1
D82	H	2-Cl	NO2	H	H	(CH2)2	bond	370/372	1
D83	H	2-Cl	CF3	Me	H	(CH2)2	bond	407/409	1
D84	H	2-Cl	CF3	OMe	H	(CH2)2	bond	423/425	1
D85	H	3,5-di-Me	H	H	H	CH2CH(Me)	bond	333	1
D86	H	3,5-di-Me	H	H	H	CH2C(Me)2	bond	347	1
D87	H	3,5-di-Me	OMe	OMe	H	(CH2)2	bond	379	1

D88	H	3,5-di-Me	H	H	Br	(CH2)2	bond	397/399	1
D89	H	3,5-di-Me	H	Br	H	(CH2)2	bond	397/399	1
D90	H	3,5-di-Me	F	H	H	(CH2)2	bond	337	1
D91	H	2,3-di-F	H	NHSO2 Me	H	(CH2)2	bond	420	1
D92	H	2-Cl	H	NHSO2 Me	H	(CH2)2	bond	418/420	1
D93	H	2,3-di-F	H	H	H	(CH2)2	bond	327	1
D94	H	3,5-di-Me	H	H	H	(CH2)2	bond	319	1
D95	H	2-Cl	OMe	OMe	H	(CH2)2	bond	385/387	1
D96	H	3,5-di-Me	NO2	H	H	(CH2)2	bond	364	1
D97	H	2-Cl	H	H	H	CH(CONH2)CH2	bond	368/370	3
D98	H	2,3-di-F	H	H	H	CH(CONH2)CH2	bond	370	3
D99	H	3,5-di-Me	H	H	H	CH(CONH2)CH2	bond	362	3
D100	H	3,5-di-Cl	H	H	H	(CH2)2	bond	359/361/363	1
D101	H	2,3,5-tri-F	H	H	H	(CH2)2	bond	343 [M-H]-	1
D102	H	3-NO2	H	H	H	CH(CH2OH)CH2	bond	366	13
D103	H	4-I	H	H	H	CH(CH2OH)CH2	bond	447	13
D104	H	4-I	H	H	H	CH(CO2H)CH2	bond	415 [M-CO2H]-	13
D105	H	4-I	H	H	H	C(=O)-C(Me)2	bond	459	15

D106	H	3-NO2	H	H	H	C(=O)-C(Me)2	bond	378	15
D107	H	3-NO2	H	H	H	C(=O)-O-	bond	352	15
D108	H	4-I	H	H	H	C(=O)-O-	bond	433	15
D109	H	3-NO2	H	H	H	CH(CH2OH)CH2 Isomer 1	bond	366	21
D110	H	3-NO2	H	H	H	CH(CH2OH)CH2 Isomer 2	bond	366	21
D111	H	4-I	H	H	H	CH(CH2OH)CH2 Isomer 1	bond	447	21
D112	H	3,5-di-F	H	H	H	CH(CH2OH)CH2 Isomer 1	bond	341	21
D113	H	4-I	H	H	H	CH(CH2OH)CH2 Isomer 2	bond	447	21
D114	H	3,5-di-F	H	H	H	CH(CH2OH)CH2 Isomer 2	bond	341	21

Table E

Encompassing compounds of general formula (XXX-6), wherein group R^2 of formula (I) is a (3-heterocyclyl) moiety (XXX-7), optionally substituted by one or more substituents R^{13} and group R^3 of formula (I) is a phenyl ring, optionally substituted by one or more substituents R^{11} and substituents R, R^1, R^{11} and R^{13} are listed in Table E.



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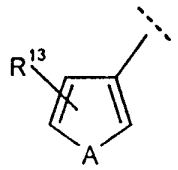


(XXX-7)

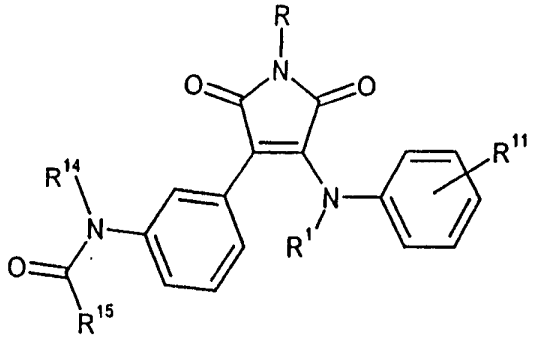
Example No.	R	R^1	R^{11}	R^{13}	A	$[M+H]^+$ Observed; (Unless $[M]^-$ or $[M-H]^-$ are Indicated)	For Procedure See Example No.
E1	H	H	3-Br	4,5-[(-CH=CH-)2]	N(Me)	396/398	4
E2	H	H	4-Me	4,5-[(-CH=CH-)2]	N(Me)	332	4
E3	H	H	4-SMe	4,5-[(-CH=CH-)2]	N(Me)	364	4
E4	H	H	3-Br-4-Me	4,5-[(-CH=CH-)2]	O	397/399	4

E5	H	H	3-Br-4-Me	H	S	363/365	4
E6	H	H	3-Cl	H	S	303/305 [M-H]-	1
E7	H	H	3,4-[S-CH=N]	4,5-[(-CH=CH-)2]	N(Me)	375	4
E8	H	H	3-OPh	4,5-[(-CH=CH-)2]	N(Me)	410	4
E9	H	H	3,4-[(CH2)3]	4,5-[(-CH=CH-)2]	N(Me)	358	4
E10	H	H	3-SMe	H	S	315[M-H]-	1
E11	H	H	4-Me	H	S	283[M-H]-	1
E12	H	H	H	H	S	269[M-H]-	1
E13	H	H	3-OPh	H	S	361[M-H]-	1
E14	H	H	3,4-[(CH2)3]	H	S	309[M-H]-	1
E15	H	H	3-Br	H	S	347/349[M-H]-	1
E16	H	H	4-SMe	H	S	315[M-H]-	1
E17	H	H	3,5-di-Br-4-OH	H	S	441/443/445[M-H]-	1
E18	H	H	3-Cl	4,5-[(-CH=CH-)2]	S	355/357	1
E19	H	H	3,5-di-Cl-4-OH	H	S	353/355/357 [M-H]-	1
E20	H	H	3,5-di-Cl-4-OH	4,5-[(-CH=CH-)2]	S	405/407/409	13
E21	H	H	3-CO2H-4-Cl	H	S	349/341	1
E22	H	H	3,4-[OCH2O]	H	S	315	1
E23	H	H	3-Cl-4-OH	H	S	319/321[M-H]-	1
E24	H	H	3,5-di-F	H	S	307	1
E25	H	H	3-CH2OH	H	S	299[M-H]-	1
E26	H	H	3-OH	H	S	287	1
E27	H	H	3,4-[OCH2O]	4,5-[(-CH=CH-)2]	S	365	1
E28	H	H	3-Cl-4-OH	4,5-[(-CH=CH-)2]	S	371/373	1
E29	H	H	3-OH	4,5-[(-CH=CH-)2]	S	337	1
E30	H	H	4-	H	S	378	1

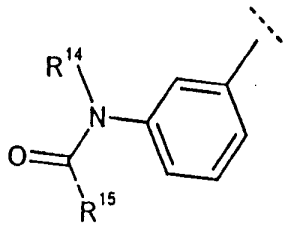
			CH2SO2NHMe				

Table F

Encompassing compounds of general formula (XXX-8), wherein group R^2 of formula (I) is a moiety of formula (XXX-9), optionally substituted by substituents R^{14} and R^{15} and group R^3 of formula (I) is a phenyl ring, optionally substituted by one or more substituents R^{11} and substituents R, R^1, R^{11}, R^{14} and R^{15} are listed in Table F.



(XXX-8)



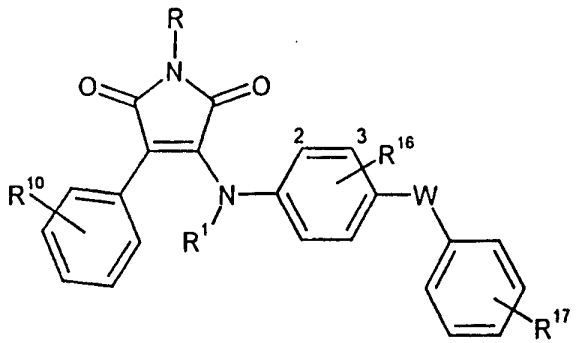
(XXX-9)

Example No.	R	R^1	R^{11}	R^{14}	R^{15}	$[M+H]^+$ Observed; (Unless $[M]^-$ or $[M-H]^-$ are Indicated)	For Procedure See Example No.
F1	H	H	3,4-[(CH2)3]	H	Me	360 [M-H]-	7
F2	H	H	3,4-[(CH2)3]	H	NH[3-F-Ph]	456 [M]-	8

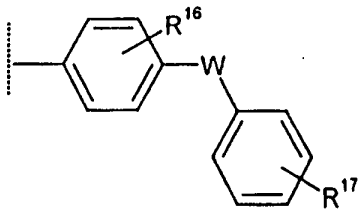
F3	H	H	3,4-[(CH2)3]	H	NH(CH2)2Ph	467	8
F4	H	H	3,4-[(CH2)3]	H	NH[Cyclohexyl]	443 [M-H]-	8
F5	H	H	3,4-[(CH2)3]	H	NHCH2CH=CH2	403	8
F6	H	H	3,4-[(CH2)3]	H	Ph	422 [M-H]-	9
F7	H	H	3,4-[(CH2)3]	H	CH2Ph	436 [M-H]-	9
F8	H	H	3,4-[(CH2)3]	H	*trans*-CH=CHPh	450	9
F9	H	H	3,4-[(CH2)3]	H	*n*-Pr	390	9
F10	H	H	3,4-[(CH2)3]	H	NHEt	389 [M-H]-	8
F11	H	H	3,4-[(CH2)3]	H	NH[3-OMe-Ph]	469	8

Table G

Encompassing compounds of general formula (XXX-10), wherein group R^2 of formula (I) is a phenyl ring, optionally substituted by one or more substituents R^{10} and group R^3 of formula (I) is a moiety of formula (XXX-11), optionally substituted by one or more substituents R^{16} and R^{17} and substituents R, R^1, R^{10}, W, R^{16} and R^{17} are listed in Table G. The position of substituent R^{16} is indicated by the locants 2 or 3 in structure (XXX-10).



(XXX-10)



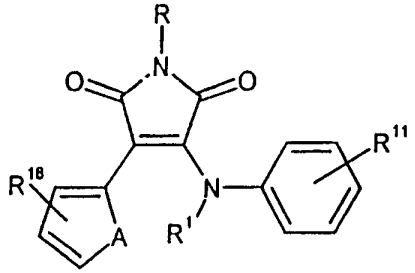
(XXX-11)

Example No.	R	R^1	R^{10}	W	R^{16}	R^{17}	$[M+H]^+$ Observed; (Unless $[M]^-$ or $[M-H]^-$ are Indicated)	For Procedure See Example No.
G1	H	H	2-OMe	S	3-CO2H	2-CO2H	491	1

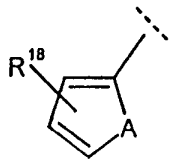
G2	H	H	4-Cl	S	H	3-CO2H	449/451 [M-H]-	1
G3	H	H	4-Cl	S	3-CO2Et	2-CO2Et	550/552 [M]-	1
G4	H	H	4-Cl	S	3-CO2Me	4-Cl	497/499/501 [M-H]-	1
G5	H	H	4-Cl	S	3-CO2H	2-CONHMe	508/510	1
G6	H	H	4-Cl	S	H	4-NO2	450/452 [M-H]-	1
G7	H	H	4-Cl	O	H	4-Cl	425/427/429	1
G8	H	H	4-Cl	S	H	2-CO2H	451/453	1
G9	H	H	4-Cl	S	3-CO2H	H	449/451 [M-H]-	1
G10	H	H	4-OMe	S	3-CO2H	2-CO2H	489 [M-H]-	1
G11	H	H	2-Cl	S	3-CO2H	2-CO2H	493 [M-H]-	1
G12	H	H	4-Cl	S	3-CO2H	3-CO2H	495/497	1
G13	H	H	2,3-di-F	S	H	3-CO2H	453	1
G14	H	H	2,3-di-F	S	3-CONHMe	2-CONHMe	523	1
G15	H	H	2,3-di-F	S	3-CO2H	2-CO2Et	523 [M-H]-	1
G16	H	H	2,3-di-F	S	H	4-CO2H	451 [M-H]-	1
G17	H	H	2,3-di-F	S	3-CO2Et	4-CO2H	525	1

Table H

Encompassing compounds of general formula (XXX-12), wherein group R^2 of formula (I) is a (2-heterocyclyl) moiety (XXX-13), optionally substituted by one or more substituents R^{18} and group R^3 of formula (I) is a phenyl ring, optionally substituted by one or more substituents R^{11} and substituents R, R^1, R^{11} and R^{18} are listed in Table H.



(XXX-12)



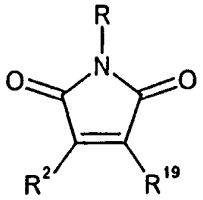
(XXX-13)

Example No.	R	R^1	R^{11}	R^{18}	A	$[M+H]^+$ Observed; (Unless $[M]^-$ or $[M-H]^-$ are Indicated)	For Procedure See Example No.
H1	H	H	3-Cl	H	S	305/307	1
H2	H	H	3-Cl	3-Me-4,5-[(-CH=CH-)2]	S	369/371	1
H3	H	H	3,5-di-Cl-4-OH	H	S	355/357/359	1

H4	H	H	3,5-di-Cl-4-OH	3-Me-4,5-[(-CH=CH-)2]	S	419/421/423	13

Table I

Encompassing compounds of general formula (XXX-14), wherein the moiety NR^1R^3 of formula (I) is represented by a general substituent R^{19} and substituents R, R^2 and R^{19} are listed in Table I.



(XXX-14)

Example No.	R	R^2	R^{19}	$[M+H]^+$ Observed; (Unless $[M]^-$ or $[M-H]^-$ are Indicated)	For Procedure See Example No.
I1	H	3-Thienyl	1-Indolinyl	297	1
I2	H	2-Thienyl	1-Indolinyl	297	1
I3	H	4-Cl-Ph	(3-Amino-1-pyridinium chloride)	301/303	19
I4	H	2-Thienyl	2-Me-Indolin-1-yl	311	1
I5	H	3-Thienyl	2-Me-Indolin-1-yl	311	1
I6	H	2,4-di-Cl-Ph	[1,3,3-Trimethyl-6-	393/395/397	1

			azabicyclo[3,2,1]octan-6-yl]		
I7	H	2,4-di-Cl-Ph	[1-Phenyl-1,3,8-triazaspiro-[4,5]-decan-4-one-8-yl]	471/473/475	1